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BRITISH MEDICAL JOURNAL

JOURNAL OF THE BRITISH MEDICAL ASSOCIATION

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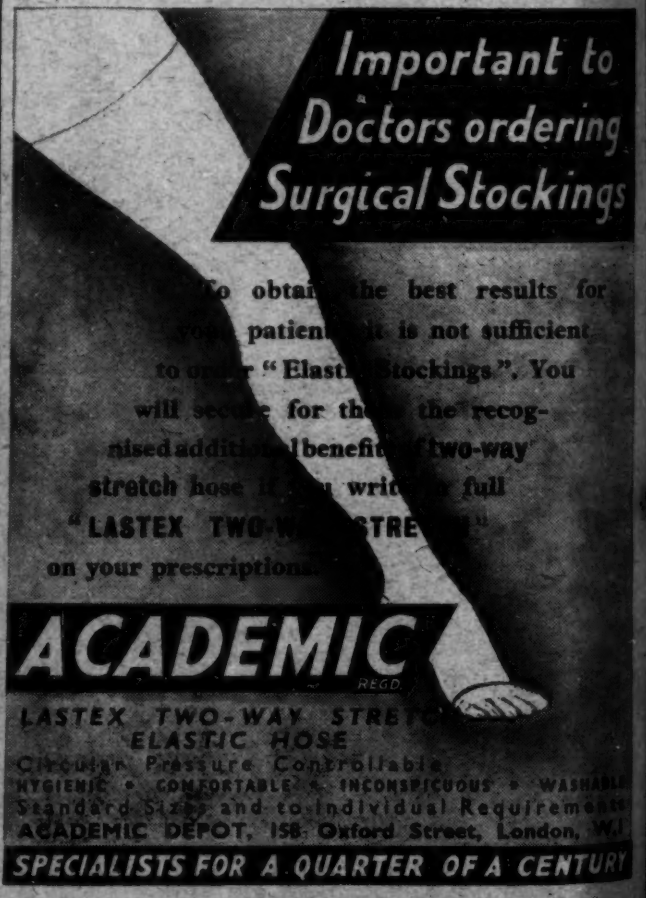
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BRITISH MEDICAL JOURNAL

LONDON SATURDAY JUNE 30 1951

THE PREVENTION OF WHOOPING-COUGH BY VACCINATION

A MEDICAL RESEARCH COUNCIL INVESTIGATION*

Since 1942 investigations have been in progress under the direction of the Whooping-cough Immunization Committee of the Medical Research Council to assess the prophylactic value of pertussis vaccines. From 1942 to 1944 controlled trials were made in Oxford City with children attending welfare clinics and day nurseries, and also in Oxfordshire, Berkshire, and Buckinghamshire with children in residential nurseries. A report of this work was published by McFarlan, Topley, and Fisher (1945). No significant difference was observed in the incidence or severity of the disease between the vaccinated and unvaccinated groups. In the Oxford City trial 12.5% of 327 vaccinated and 14.1% of 305 unvaccinated children developed pertussis, while in those residential nurseries in which whooping-cough occurred 55% of 33 vaccinated children and 63% of 30 unvaccinated children were attacked. Similar unfavourable results have been reported by others. Doull and his colleagues (1939) described a trial, comprising 479 vaccinated and 496 unvaccinated children who were the older siblings of the former, in which the numbers of cases of pertussis in the two groups were 74 and 94 respectively. Siegel and Goldberger (1937), in a trial in a tuberculosis sanatorium, reported attack rates in children exposed to the disease of 53% in the vaccinated and 58% in the unvaccinated groups.

On the other hand, the majority of vaccination studies, most of which were made in the United States of America and Canada, indicated that pertussis vaccine produced a significant degree of protection. Many of these studies were reviewed by Felton and Willard (1944) and by Tudor Lewis (1946). The first hopeful results were observed by Zachariassen (see Madsen, 1933) in two epidemics in the Faroe Islands. A plain vaccine was used prepared from freshly isolated strains of *Haemophilus pertussis*. In the first epidemic, vaccination was begun during the outbreak and was found to have no effect on incidence, although it was reported to have reduced the severity of the disease. In the second epidemic, vaccination was completed shortly before the outbreak occurred, and of the 1,832 vaccinated children 75% contracted pertussis, compared with 98.2% among the 446 unvaccinated children. Encouraging results were later obtained by Sauer (1937), who used a plain vaccine prepared from strains which fulfilled the criteria for phase I *H. pertussis* described by Leslie and Gardner (1931). In this investigation Sauer vaccinated 1,122 children, and reported that of 128 who were subsequently exposed to pertussis, 94 in their own homes, only six developed the disease. Of the many studies made with plain vaccine the best known are those conducted by Kendrick and Eldering (1939). These studies comprised a total of 4,212 children, divided into vaccinated and unvaccinated groups which were similar in a number of respects. Of children exposed to infection in the home 34.9% in the vaccinated group contracted pertussis compared with 89.4% in the unvaccinated group.

In the majority of studies with plain vaccine the total dosage was relatively large in volume (sometimes 7 ml.) and in numbers of organisms (70 to 120 thousand million), and was given in three to five injections. More recently investigations have been made to determine whether effective protection could be obtained with alum-precipitated pertussis vaccine when given in smaller doses than those used with plain vaccines. Bell (1941, 1948) made two well-controlled trials, the first with alum-precipitated vaccine alone and the second with alum-precipitated combined pertussis vaccine and diphtheria toxoid. In each trial the total dose of vaccine was 20 thousand million organisms, given in two inoculations at an interval of four weeks. The incidence of the disease among the unvaccinated children was three to four times greater than that among the vaccinated. Kendrick (1942, 1943) also obtained good results with an alum-precipitated vaccine which was given in three doses.

In view of these favourable reports the Whooping-cough Immunization Committee concluded that the vaccines used in their trials in 1942–4 differed in some material though unknown way from those vaccines which had been shown to give protection. The Committee therefore decided to carry out a new series of

*The following collaborated in this investigation:

Members of the Whooping-cough Immunization Committee of the Medical Research Council: Professor S. P. Bedson, F.R.S. (chairman), Dr. W. C. Cockburn, Dr. E. T. Conybeare, Professor R. Cruickshank, Professor A. W. Downie, Professor A. Bradford Hill, Dr. P. L. Kendrick, Dr. J. Knowelden, Professor J. W. McLeod, F.R.S., Dr. H. J. Parish, Mr. A. F. B. Standfast, Dr. G. S. Wilson, Dr. D. G. Evans (secretary).

Medical Officers of Health: The late Dr. G. C. Williams (Oxford); Dr. C. Metcalfe Brown (Manchester); Dr. F. Roy Dennison (West Ham); Dr. G. Hamilton Hogben (Tottenham); the late Dr. A. G. Morison and Dr. E. Grundy (Wembley); Dr. J. Johnstone Jervis, Dr. J. F. Warin (Deputy M.O.H.), and Dr. I. G. Davies (Leeds); Dr. D. Regan (Edmonton).

Field Workers: Dr. M. Fisher and Miss C. Rudkin (Oxford); Dr. A. V. Magee and Miss O. I. Howell (Manchester); Dr. W. C. Cockburn, Miss M. A. Massey, and Miss M. M. Wall (Wembley, Tottenham, and Edmonton); Dr. G. R. Baxter and Mrs. E. R. Beard (Leeds); Dr. F. Barasi and Mrs. L. J. Bunch (West Ham).

Laboratory Workers: Dr. R. Knox (Oxford); Dr. H. W. Clegg, Dr. H. R. Cayton, and Dr. M. T. Parker (Manchester); Dr. A. J. H. Tomlinson and Dr. H. D. Holt (Colindale); Professor J. W. McLeod, Mrs. E. H. Farnworth, and Dr. B. Dawson (Leeds); Dr. W. W. Walther (West Ham).

The trials were planned with the advice of the Statistical Research Unit of the Medical Research Council and were arranged and supervised by Dr. W. C. Cockburn.

The results were analysed and the report prepared by Dr. W. C. Cockburn, Dr. D. G. Evans, and Dr. J. Knowelden.

field trials with a number of vaccines prepared in different laboratories and to include vaccines of American origin which in previous studies had been reported to give substantial protection.

The first trial in this new series was in Oxford City. Three batches of Sauer vaccine, prepared by Messrs. Parke Davis & Co., of Detroit, were tested. In all, 1,530 children between the ages of 6 months and 5 years were inoculated, 785 with pertussis vaccine and 745 with "anticatarrhal" vaccine containing no *H. pertussis*. After inoculation the children were observed for a period of two to three years. The total number of definite cases of pertussis diagnosed in those children who received pertussis vaccine was 113 and in those who received "anticatarrhal" vaccine 165, giving attack rates per 1,000 child-months of observation of 5.28 and 8.17 respectively. In addition to these definite cases there were 143 doubtful cases—80 in the group which received pertussis vaccine and 63 in the comparative group. This trial was begun during the war, in 1944, when it was impossible to obtain adequate staff to deal with intensive follow-up investigations. Further, the staff necessary and the number of visits required to ensure the standard of accuracy needed in these trials were, at this early stage, underestimated by the Committee. The follow-up studies, therefore, were in many cases incomplete. For this reason the Committee does not propose to draw any firm conclusions from the results of this early trial, though it appears unlikely that the vaccines were highly effective. The trial, however, provided invaluable information regarding the problems associated with organization, and the subsequent trials, reported below, were planned in the light of experience gained in the Oxford investigation.

General Plan of Investigation

In all trials a uniform plan was followed. Children between the ages of 6 and 18 months, whose parents agreed that they should be inoculated, were divided by the method of random sampling into two groups of approximately equal size. *The children in one group were inoculated with pertussis vaccine and are referred to subsequently as "vaccinated." Those in the other group were given a similar dose of "anticatarrhal" vaccine which contained no H. pertussis and are referred to subsequently as "unvaccinated."* After inoculation each child was visited at frequent intervals for a period of two to three years by a nurse-investigator. Neither the parents nor the observers knew whether a child was in the vaccinated or the unvaccinated group.

Five batches of pertussis vaccine from three manufacturers—Messrs. Parke Davis & Co., of Detroit, the Michigan Department of Health, and Messrs. Glaxo Laboratories Ltd.—were used in ten separate field trials in Leeds, Manchester, Tottenham and Edmonton, Wembley, and West Ham. Information on the nature and dosage of the vaccines and the areas to which they were allocated is given in Table I. The "anticatarrhal" vaccine was prepared specially for the inquiry by Messrs. Burroughs Wellcome & Co. It contained killed suspensions of *Staphylococcus aureus, Streptococcus pneumoniae, Corynebacterium hofmannii, and Neisseria catarrhalis*, and was similar in turbidity to the plain pertussis vaccines. It was dispensed in the same type of bottle as that used for the pertussis vaccines.

Procedure in the Field

In each trial area a "pertussis team" was appointed comprising a full- or part-time medical officer, a nurse-investigator for each group of 400–500 children, and a full- or part-time clerk. The members of the teams in most areas were appointed from the staff of the local health department who had had close associations in their routine work with mothers of young children and experience in the administration and day-to-day work of diphtheria immunization schemes. Where it was not possible to make such arrangements the teams were appointed by the Committee in collaboration with the medical officer of health.

Propaganda

Parents with children aged 6–18 months were given a pamphlet, to which was attached a parent's consent form, explaining the scheme. The pamphlet was either sent by post, distributed at welfare centres, or handed to the mothers by a health visitor on her routine visits. In the pamphlet it was made clear that the vaccines were being tested, that it was necessary to inoculate some of the children with a substance which was not whooping-cough vaccine, and that parents and observers would not know until the end of the investigation whether a child was in the vaccinated or the unvaccinated group. In addition, posters were displayed in welfare centres and nursery schools, and in some areas the medical officers of health publicized the scheme with the help of the Press, the cinema, and the radio. A letter was sent to all general practitioners in the area giving them details of the plan and inviting them to co-operate by giving advice on the scheme to parents and by informing the health department of suspected cases of pertussis among trial children under their care.

TABLE I.—*Trial Areas, Vaccines, and Dosage Schedules*

Trial Area	Vaccine				Dosage Schedule	
	Batch	Manufacturer	Description	Conc. in Millions of Organisms/ml. (American Count)*	Doses at Monthly Intervals (ml.)	Total Dose in Millions of Organisms
Manchester	Sauer 087860	Parke Davis & Co., Detroit	Plain suspension	15,000	1, 2, 3	90,000
Manchester, Tottenham and Edmonton, Wembley	Michigan D231	Michigan Dept. of Health	" "	10,000	1, 2, 3	60,000
Leeds	Glaxo 61	Glaxo Laboratories	Alum precipitated	50,000	0·75, 0·75, 0·75	112,000
Leeds	Glaxo 174	" "	" "	50,000	0·75, 0·75, 0·75	112,000
West Ham	Glaxo 174	" "	" "	50,000	0·5, 0·5, 1	100,000
Manchester, Tottenham and Edmonton, Wembley	Michigan A236	Michigan Dept. of Health	Plain suspension	10,000	1, 2, 3	60,000

* Concentrations of all vaccines are given in terms of the American count, as British and American vaccines, with the same labelled concentration, differ considerably in density (see McFarlan, Topley, and Fisher, 1945).

Allocation of Children to the Vaccinated and Unvaccinated Groups

On receipt of signed consent forms from the parents, children with no previous history of pertussis or of previous inoculation with pertussis vaccine were classified by sex and placed in one of the following age groups: 6–8, 9–11, 12–14, and 15–17 months; a few children were accepted just after they had reached the age of 18 months. For each age and sex group, sheets were previously drawn up on which vaccine letters A, B, C, and D in random order were repeated a sufficient number of times to deal with all expected volunteers in the appropriate age and sex group. As each child's name was received it was written in the first vacant space on the appropriate sheet, and the vaccine letter opposite the child's name determined what it should receive and was inserted on the child's record card.

Although four vaccine letters were used, two of them in fact indicated the pertussis vaccine being tested in the trial and the other two the "anticatarrhal" vaccine. It was thought that by employing this method field-workers would be less likely to distinguish the pertussis vaccine from the "anticatarrhal" vaccine. As the early trials progressed it became evident that more cases of pertussis were occurring in children inoculated with vaccines A and C—the "anticatarrhal" vaccines—than in children with vaccines B and D—the pertussis vaccines. There was also some difference in the incidence of slight inoculation reactions between the pertussis and "anticatarrhal" vaccines. To ensure, therefore, that follow-up observations remained unbiased, the vaccine letter on each record card was covered by a thick label until the end of the investigation or until the duration and severity of an attack of pertussis had been recorded on the card.

Inoculation of Children

When sufficient names had been obtained, clinic sessions were arranged on an appointment system. On arrival at the clinic the children were inoculated with vaccine from the bottle labelled with the appropriate vaccine letter. Three inoculations were given at monthly intervals. In general the inoculations were given intramuscularly, although in some areas at the beginning of the trials they were given subcutaneously. One child in every five was visited 24–72 hours after each inoculation to determine the severity of the reaction.

If a child failed to attend for the first inoculation, a second and, if necessary, a third appointment was arranged, and if these were not kept, no further steps were taken and the child was excluded from the trial. Further appointments were also made for those children who failed to attend for the second or third inoculation, and if they still failed to attend they were visited to ascertain the reason. In most cases a satisfactory reason was obtained.

When each child received the last inoculation the mother was given a report slip in a stamped envelope addressed to the health department and was instructed to post this slip if the child had been in contact with whooping-cough or had developed suspicious symptoms.

Follow-up Observations

When the course of inoculations was completed each child was visited monthly by a nurse-investigator until the end of the investigation or until it was excluded from the trial. On the first visit the information already entered on the record card was checked and notes were made of the duration of breast-feeding and of the number of other children under 14 years of age living in the house. On subsequent monthly visits information was obtained on exposures to pertussis, the incidence of upper respiratory-tract infections, the history of diphtheria immunization and smallpox vaccination, and the incidence of measles, chicken-pox, bronchopneumonia, and diphtheria.

When it was found, either on a routine visit or by receipt of the report slip from the parent, that a child had been exposed to pertussis or had developed suspicious symptoms, repeated visits were made to determine the diagnosis and to assess the severity of the attack if it proved to be pertussis. So far as possible these special visits were made by the senior nurse-investigator or by the medical member of the pertussis team. During the special visits a detailed history of the intimacy and duration of exposure was obtained and, where possible, nasopharyngeal swabs were taken. Sometimes swabs were also taken from the presumed infecting case. The mother was asked to make notes of the number of paroxysms during each 24 hours at the height of the disease. Notes were also made by the observers of the nature and severity of complications. At the end of the illness the degree of severity of the attack (see footnote to Table VII) and the duration of the cough were recorded.

Once children who had developed pertussis were considered to have made a complete recovery, nurse-investigators were not required to visit them more often than every three months, although in fact in most areas it was found convenient to continue the monthly visits. These visits were necessary to obtain information on diphtheria immunization, on smallpox vaccination, and on the incidence of other infectious diseases.

Number of Children and Duration of Trials

The number of children whose parents agreed to take part in the investigation was 8,927, of whom 4,515 were allocated to the vaccinated and 4,412 to the unvaccinated group (Table II). Of these, 7,558 completed the course of inoculations—3,801 in the vaccinated and 3,757 in the unvaccinated group. Most of the remainder, 1,369 in all, were children whose parents repeatedly failed to

TABLE II.—*Numbers of Children in All 10 Trials*

	Vaccinated (Inoculated with Pertussis Vaccine)			Unvaccinated (Inoculated with "Anticatarrhal" Vaccine)			Total
	Male	Female	Both Sexes	Male	Female	Both Sexes	
Total children entered for inoculation	2,182	2,333	4,515	2,273	2,139	4,412	8,927
Excluded before completion of inoculations*	359	355	714	341	314	655	1,369
Total number given 3 inoculations	1,823	1,978	3,801	1,932	1,825	3,757	7,558
Excluded during follow-up period†	218	225	443	213	192	405	848
Total number remaining at end of follow-up period	1,605	1,753	3,358	1,719	1,633	3,352	6,710

* Persistent defaulters; developed or were in contact with pertussis; moved from area; illness or death not associated with pertussis or inoculation.
† Moved from area; reinoculated by private doctor; death not associated with pertussis or inoculation; uncooperative parents. Observations on these children, up to the time when they were lost from the investigation, were included in the analysis.

keep appointments for the first inoculation. After the first inoculation few parents defaulted, and those that did had good reasons, such as prolonged illness in the child or removal from the trial area. The period for observation began as soon as each child received its third inoculation. After the completion of inoculations, 848 children were lost from observation at varying intervals, in most cases because they left the area. Other reasons for withdrawal are given in the footnote to Table II. Observations on these children, up to the time when they were lost from the investigation, were included in the analysis. At the end of the investigation 6,710 children remained; 3,358 were in the vaccinated and 3,352 in the unvaccinated group.

Trials were begun between November, 1946, and April, 1948, and were completed during 1950. In all trials, except that in West Ham, the inoculations were given within a period of three to six months; in West Ham most of the children were inoculated during the first year of the investigation. On the average, each child was observed for 27 months after its third inoculation; the average period varied from 23 to 30 months in the separate trials. The period of each trial in relation to the incidence of notified cases of pertussis in the general population is shown in the Chart.

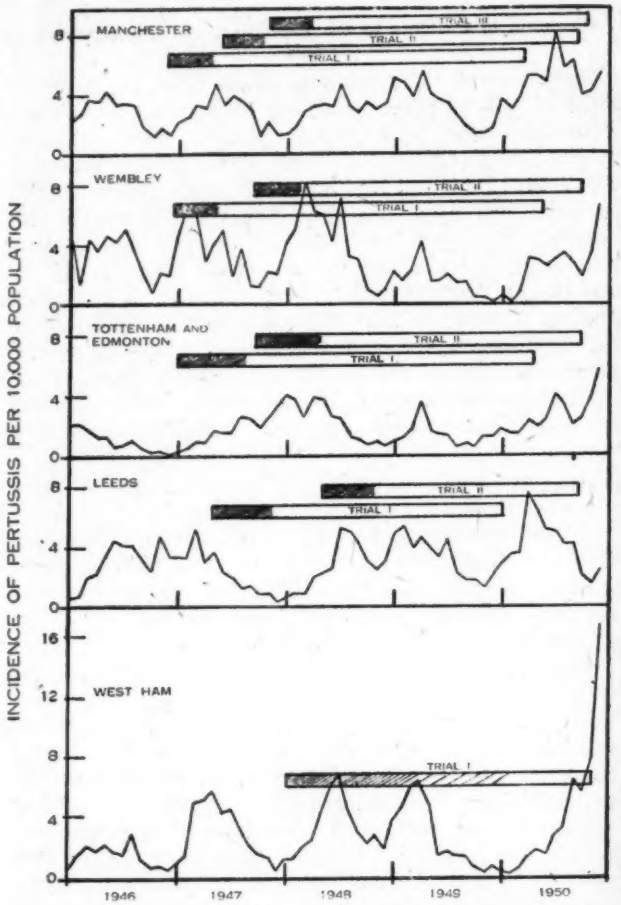

Chart showing notified incidence of pertussis per 10,000 population (all ages), from 1946 to 1950, in the trial areas. The horizontal blocks indicate the period of the trials and the shaded areas the period during which the inoculations were given. In the West Ham trial the densely shaded area indicates the period during which the majority of children were inoculated.

Similarity of Vaccinated and Unvaccinated Groups

The method of allocation of the children to vaccinated and unvaccinated groups was found, by examining certain relevant attributes of the children, to give two groups of closely similar character. It is clear from Table III, which relates to all 10 trials, that the two groups were similar in the number of children, their average age, the average number of children (including the trial child) under 14 years of age in the families, and the average duration of the period over which they were observed. Furthermore, the similarity of the two groups was evident from the information relating to breast-feeding, infectious diseases other than pertussis, immunization against diphtheria, and vaccination against smallpox. In each separate trial also, the two groups were similar in character.

Reactions to Inoculations

One child in every five in the vaccinated and unvaccinated groups was visited 24–72 hours after each inoculation. With the plain vaccines no severe local or general reactions were observed, although a number of children developed a rise in temperature within 24 hours of inoculation, and in some the site of inoculation was red and swollen for one to two days. In only a few instances were the reactions such that the mother refused to co-operate further. There was no apparent increase in the incidence of reactions after the second

TABLE III.—*Similarity of Vaccinated and Unvaccinated Groups in All 10 Trials*

	Vaccinated			Unvaccinated			Grand Total
	Male	Female	Total	Male	Female	Total	
Total No. of children given 3 inoculations	1,823	1,978	**3,801**	1,932	1,825	**3,757**	7,558
Average age (months)	12·1	12·3	**12·2**	12·2	12·2	**12·2**	12·2
Average duration of observation per child (months)	26·9	27·2	**27·1**	27·2	27·2	**27·2**	27·1
Average No. of children under 14 years per household	1·8	1·8	**1·8**	1·8	1·8	**1·8**	1·8
Breast-feeding:							
No. breast-fed	1,457	1,575	**3,032**	1,540	1,471	**3,011**	6,043
Average duration of breast-feeding (months)	5·4	5·3	**5·3**	5·3	5·4	**5·4**	5·4
No. not breast-fed	321	350	**671**	344	308	**652**	1,323
No. where history not known	45	53	**98**	48	46	**94**	192
No. of cases of certain other infectious diseases in children during the trial:							
Measles	440	480	**920**	471	420	**891**	1,811
Chicken-pox	138	151	**289**	139	141	**280**	569
Bronchopneumonia	50	45	**95**	53	41	**94**	189
Diphtheria	0	1	**1**	1	0	**1**	2
Total	628	677	**1,305**	664	602	**1,266**	2,571
No. known to be:							
Immunized against diphtheria	1,592	1,736	**3,328**	1,716	1,609	**3,325**	6,653
Vaccinated against smallpox	1,151	1,240	**2,391**	1,205	1,141	**2,346**	4,737

and third inoculations. In trial areas where alum-precipitated vaccines were used, six children developed sterile abscesses.

Byers and Moll (1948), Toomey (1949), and others, in the United States of America, and Anderson and Morris (1950), in this country, reported the occurrence of convulsions and encephalopathies as rare complications of pertussis vaccination. Martin (1950), McCloskey (1950), Geffen (1950), and Bradford Hill and Knowelden (1950) drew attention to the occurrence of poliomyelitis in which the paralysis affected with undue frequency the limb which had recently been injected with diphtheria or pertussis or with the combined prophylactic. These reports were made while the present studies were in progress, and the records of all children who had completed the course of inoculations were carefully scrutinized and most of the children who had not completed the course were revisited. None of the children had a history of convulsions, and in none did poliomyelitis develop within the arbitrarily chosen period of two months after inoculation. In only two trials—Manchester II and Leeds I—were the children inoculated during periods of high incidence of poliomyelitis, and as the numbers of children were relatively small the risk of any one child developing poliomyelitis was remote.

Incidence and Severity of Pertussis

Attack Rates Per 1,000 Child-months of Observation

In all ten trials the total number of cases of pertussis diagnosed in the vaccinated groups was 149 and in the unvaccinated groups 687 (Table IV). The corresponding attack rates per 1,000 child-months of observation were 1.45 and 6.72—a ratio of 1:4.6. This difference in attack rates is clearly significant. In both vaccinated and unvaccinated groups the attack rates in females were higher than in males, an observation in agreement with previous epidemiological studies.

It is also evident (Table V) that in each separate trial the attack rate in the vaccinated was substantially less than in the unvaccinated group, but the ratio of the attack rates was not the same for all trials. These differences in ratios are taken into account when comparing the potency of vaccines (Table XIV).

Attack Rates in Children Known to Have Been Exposed to Pertussis

Analysis of information on the exposure of the children to pertussis showed that such occurrences could be conveniently divided into two categories: (1) "Home exposures"—children exposed in their own homes to infection in one or more siblings; (2) "other exposures"—children exposed to infection in day nurseries, in nursery schools, at parties, in cinemas, in buses, and while playing outside the home with other children. The figures for each of these categories are given for each trial and also for all 10 trials (Table VI). In the table the number of exposures to pertussis is recorded, not the number of children exposed, as some children were exposed on more than one occasion. Exposure to infection could also occur *after* a child in the trial had developed pertussis, but such exposures were not recorded.

The average attack rate in the "home exposures" for all 10 trials was 18.2% in the vaccinated and 87.3% in the unvaccinated groups. A high incidence of pertussis occurred in the unvaccinated group of each trial; in only one trial was the attack rate less than 75%. The attack rates in the vaccinated groups varied considerably with the different trials, and this variation is considered when comparing the potency of the vaccines (Table XIV).

With the "other exposures," the average attack rate for all 10 trials was 8.3% in the vaccinated and 38.0% in the unvaccinated groups. In this category the attack rates in both groups varied, but the variation was not as great in the unvaccinated as in the vaccinated groups.

A history of exposure was not obtained for every case, and 65 children in the vaccinated and 323 in the

TABLE IV.—*Number of Cases of Pertussis and Attack Rates per 1,000 Child-months of Observation in Vaccinated and Unvaccinated Groups in All 10 Trials*

	Vaccinated				Unvaccinated			
	No. of Children given 3 Inoculations	Duration of Observation* (Child-months)	Cases of Pertussis	Attack Rate per 1,000 Child-months	No. of Children given 3 Inoculations	Duration of Observation* (Child-months)	Cases of Pertussis	Attack Rate per 1,000 Child-months
Males	1,823	49,105	68	1·38	1,932	52,472	327	6·23
Females	1,978	53,856	81	1·50	1,825	49,708	360	7·24
Both sexes	3,801	102,961	149	1·45	3,757	102,180	687	6·72

* Observation began from the date of the third inoculation.

TABLE V.—*Number of Cases of Pertussis and Attack Rates per 1,000 Child-months of Observation in Vaccinated and Unvaccinated Groups in Each Trial*

Trial Area	Area-trial No.	Vaccine	Vaccinated				Unvaccinated			
			No. of Children given 3 Inoculations	Duration of Observation (Child-months)	Cases of Pertussis	Attack Rate per 1,000 Child-months	No. of Children given 3 Inoculations	Duration of Observation (Child-months)	Cases of Pertussis	Attack Rate per 1,000 Child-months
Manchester ..	I	Sauer 087860	415	12,125	32	2·64	449	13,241	89	6·72
Tottenham and Edmonton	I	Michigan D231	167	4,394	3	0·68	183	4,726	33	6·98
Wembley ..	I	Michigan D231	142	3,680	2	0·54	144	3,828	33	8·62
Manchester ..	II	Michigan D231	321	9,522	12	1·26	328	9,762	63	6·45
Leeds	I	Glaxo 61	489	13,392	27	2·02	464	12,864	85	6·61
Leeds	II	Glaxo 174	484	11,488	25	2·18	425	10,215	97	9·50
West Ham ..	I	Glaxo 174	727	16,768	29	1·73	771	17,464	92	5·27
Manchester ..	III	Michigan A236	460	13,445	11	0·82	458	13,828	94	6·80
Tottenham and Edmonton	II	Michigan A236	306	9,307	5	0·54	257	7,471	49	6·56
Wembley ..	II	Michigan A236	290	8,840	3	0·34	278	8,781	52	5·92
Totals			3,801	102,961	149	1·45	3,757	102,180	687	6·72

TABLE VI.—*Number of Cases of Pertussis and Percentage Attack Rates by Type of Exposure in Vaccinated and Unvaccinated Groups in Each Trial*

Trial Area	Area-trial No.	Vaccine	"Home Exposures"						"Other Exposures"						No. of Cases with no History of Exposure	
			Vaccinated			Unvaccinated			Vaccinated			Unvaccinated				
			No. of Exposures	No. of Cases	% Cases/ Exposures	No. of Exposures	No. of Cases	% Cases/ Exposures	No. of Exposures	No. of Cases	% Cases/ Exposures	No. of Exposures	No. of Cases	% Cases/ Exposures	Vaccinated	Unvaccinated
Manchester..	I	Sauer 087860	36	8	22·2	20	17	85·0	100	15	15·0	73	24	32·9	9	48
Tottenham and Edmonton	I	Michigan D231	12	0	0	15	14	93·3	20	1	5·0	21	9	42·9	2	10
Wembley ..	I	Michigan D231	9	1	11·1	12	8	66·7	33	0	0	42	12	28·6	1	13
Manchester..	II	Michigan D231	20	2	10·0	12	9	75·0	78	5	6·4	65	26	40·0	5	28
Leeds ..	I	Glaxo 61	23	7	30·4	21	19	90·5	69	6	8·7	71	29	40·8	14	37
Leeds ..	II	Glaxo 174	29	7	24·1	24	21	87·5	60	9	15·0	72	28	38·9	9	48
West Ham ..	I	Glaxo 174	18	7	38·9	19	18	94·7	23	4	17·4	36	22	61·1	18	52
Manchester..	III	Michigan A236	26	3	11·5	21	19	90·5	112	6	5·4	90	35	38·9	2	40
Tottenham and Edmonton	II	Michigan A236	14	2	14·3	16	15	93·8	26	1	3·8	22	12	54·5	2	22
Wembley ..	II	Michigan A236	16	0	0	13	11	84·6	45	0	0	69	16	23·2	3	25
Totals			203	37	18·2	173	151	87·3	566	47	8·3	561	213	38·0	65	323

unvaccinated groups developed pertussis without the source of infection being known.

It is of interest that in the "home exposures," the "other exposures," and in children with no history of exposure the ratios of the incidence of pertussis in the vaccinated to that in the unvaccinated children was almost identical—namely, 1:4.8, 1:4.6, and 1:5.0.

Severity and Duration of Attack

The assessment of the degree of severity of attack was based, in general, on the parent's record of the number of paroxysms in 24 hours during the height of the disease (see footnote to Table VII). Parents varied in their ability to keep accurate records of the number of paroxysms and, in any event, no record could be made of the severity of each paroxysm. As a general guide to severity of attack, however, the method was valuable, particularly as neither parents nor members of the team knew whether any one child suffering from the disease was in the vaccinated or the unvaccinated group.

TABLE VII.—*Degree of Severity of Attack in Diagnosed Cases of Pertussis in All 10 Trials*

	Vaccinated (149 Cases)					Unvaccinated (687 Cases)					
	Degree of Severity*					Degree of Severity*					
	1	2	3	4	5	1	2	3	4	5	Not Stated
No. of cases ..	32	77	29	9	2	17	148	281	212	28	1
Percentage	21·5	51·7	19·5	6·0	1·3	2·5	21·6	40·9	30·9	4·1	
	73·2		26·8			24·1		75·9			

* 1 = An abortive attack, with or without occasional paroxysms confirmed bacteriologically. 2 = Fewer than 10 paroxysms in 24 hours at height of disease. 3 = 10–20 paroxysms in 24 hours at height of disease. 4 = More than 20 paroxysms in 24 hours at height of disease. 5 = Attack complicated by bronchopneumonia, atelectasis, etc.

The severity of attack for cases in both the vaccinated and the unvaccinated groups for all 10 trials is given in Table VII. Degrees of severity of 1 and 2 may be considered as mild, and 3, 4, and 5 as moderate, severe, and complicated attacks. In the vaccinated 73.2% of cases were mild compared with 24.1% in the unvaccinated groups. Two complicated cases occurred in the vaccinated, compared with 28 in the unvaccinated. There were no deaths in either group.

An additional indication of severity was obtained by recording the duration of the cough (Table VIII). By this method also, a difference between the two groups was observed: 44.3% of cases in the vaccinated had a cough for less than six weeks, compared with 14.4% in the unvaccinated groups.

Similar differences in severity and duration of attack between vaccinated and unvaccinated children were observed when each trial was considered separately.

TABLE VIII.—*Duration of Cough in Diagnosed Cases of Pertussis in All 10 Trials*

	Vaccinated (149 Cases)					Unvaccinated (687 Cases)					
	Duration (Weeks)					Duration (Weeks)					
	Under 4	4–	6–	8–	10+	Under 4	4–	6–	8–	10+	Not Stated
No. of cases ..	20	46	47	15	21	15	82	178	159	240	13
Percentage	13·4	30·9	31·5	10·1	14·1	2·2	12·2	26·4	23·6	35·6	
	44·3		55·7			14·4		85·6			

Duration of Immunity

An analysis was made which indicated that during the period of observation there was no waning in the degree of protection afforded by the pertussis vaccines. Attack rates at intervals after inoculation are given in Table IX for those vaccinated and unvaccinated children who were exposed to infection in their own homes. It is evident that the attack rate in the unvaccinated children was almost constant during the whole period of observation, and it is therefore justifiable to compare the corresponding attack rate in the vaccinated children. Throughout the period of observation the attack rate in the vaccinated children remained at approximately 20% and showed no evidence of increasing even two years after inoculation.

TABLE IX.—*Percentage Attack Rates in "Home Exposures" at Intervals After Inoculation in Vaccinated and Unvaccinated Children in All 10 Trials*

Period after Third Inoculation (Months)	Vaccinated			Unvaccinated		
	No. of Exposures	No. of Cases	% Cases/ Exposures	No. of Exposures	No. of Cases	% Cases/ Exposures
0–5 ..	54	8	15	49	44	90
6–11 ..	50	10	20	45	38	84
12–17 ..	36	6	17	41	39	95
18–23 ..	36	8	22	22	18	82
24 and over	27	5	19	16	12	75
Totals ..	203	37	18	173	151	87

A further analysis was made for each of the five vaccines separately, and for none of them, within the limits of the small numbers of cases involved, was there evidence of waning immunity during the period of observation.

Occurrence of Coughs not Diagnosed as Pertussis After Exposure to Infection

After reported exposure to pertussis particular attention was paid to all children for a period of 42 days. During this period a number of children developed a cough which was not paroxysmal in character. Most of those in whom the cough lasted for more than a week were swabbed. The average number of swabs taken from each child was 1.5. From some of these cases *H. pertussis* was isolated, and they were recorded as cases of pertussis with a degree of severity of 1, but in the majority no bacteriological evidence of pertussis infection was obtained.

The duration of the cough in these cases is given in Table X. It is evident that in 90% of the children the cough was of short duration, lasting for less than four weeks, and that there was no pronounced difference between the vaccinated and unvaccinated groups in its average duration. Further, from Table XI it is evident that the incidence of this type of cough in those who were exposed to pertussis but did not develop it was similar in both groups. For these reasons it was considered that most of these cases were not due to infection with *H. pertussis*.

TABLE X.—*Duration of Cough in Children Who Did Not Develop Pertussis but Who had a Cough which Began Between 7 and 42 Days After Known Exposure to Pertussis*

	Vaccinated (231 Children)					Unvaccinated (129 Children)				
	Duration (Weeks)					Duration (Weeks)				
	Under 2	2–	3–	4–	5+	Under 2	2–	3–	4–	5+
No. of cases	111	61	29	20	10	45	46	27	5	6
Percentage ..	48·0	26·4	12·6	8·7	4·3	34·9	35·6	20·9	3·9	4·7
	87·0			13·0		91·4			8·6	

TABLE XI.—*Incidence of Cough in Children who Did Not Develop Pertussis After Exposure*

	Vaccinated	Unvaccinated
Total No. of "home" and "other" exposures	769	734
No. of exposures followed by pertussis ..	84	364
No. of exposures not followed by pertussis ..	685	370
No. of cases of cough not diagnosed as pertussis	231	129
Percentage of cases of cough in exposures not followed by pertussis	34	35

Bacteriological Observations

Swabs were taken from 806 (96.4%) of the 836 clinically diagnosed cases (Table XII). Postnasal swabs were used in the early stages of the investigation, but later it was found that pernasal swabs gave better results (Cockburn and Holt, 1948) and these were then used in all areas. So far as possible the swabs were obtained in the first two weeks of the disease and the average number of swabs per child was 1.85 for all trials; the figures for the separate trials are also given in Table XII. *H. pertussis* was isolated from 59.8% of the cases which were swabbed and from 57.7% of all cases diagnosed. The proportion of clinical cases confirmed bacteriologically varied from area to area, but the percentage in the vaccinated was similar to that in the unvaccinated group for each trial and for all trials together (Table XIII).

TABLE XIII.—*Number and Percentage of Bacteriologically Confirmed Cases in Vaccinated and Unvaccinated Groups in All 10 Trials*

Vaccinated			Unvaccinated		
Cases of Pertussis	Confirmed Bacteriologically		Cases of Pertussis	Confirmed Bacteriologically	
	No.	%		No.	%
149	83	55·7	687	399	58·1

Haemophilus parapertussis was isolated from 24 children with clinical symptoms of pertussis. None of these cases occurred in Tottenham and Edmonton, nine were in West Ham, and the remainder were distributed in the other trial areas. There were 10 cases in the vaccinated and 14 in the unvaccinated group. Nearly all were mild; in 21 the degree of severity was 3, and in 18 the cough lasted less than six weeks. *Haemophilus bronchisepticus* was isolated from one case with clinical symptoms of pertussis which occurred in Leeds. The child had a cough for six weeks and the degree of severity was estimated as 3. There have been previous reports of the isolation of *H. parapertussis* from cases clinically diagnosed as pertussis (Bradford and Slavin, 1937; Eldering and Kendrick, 1938; Miller *et al.*, 1941; Cruickshank and Knox, 1946; Sohier and Fauchet, 1949), and a case, with symptoms of pertussis, from which *H. bronchisepticus* was isolated has also been described (Brown, 1926).

Serological tests were made in a number of children in both the vaccinated and unvaccinated groups at varying intervals after inoculation and the results will be referred to in a later report.

Comparison of the Prophylactic Potency of the Vaccines

It is not possible from the results of these trials to make a direct comparison of the prophylactic potency of the vaccines, as they were not tested in the same area

TABLE XII.—*Number and Percentage of Cases From Which H. pertussis was Isolated by Swab Culture in Both Vaccinated and Unvaccinated Groups in Each Trial*

Trial Area	Area-trial No.	Vaccine	Cases of Pertussis	No. of of Cases Swabbed	Average No. of Swabs per Swabbed Child	No. of Cases giving Pos. Swab	Percentage of Total Cases giving Pos. Swab	Percentage of Swabbed Cases giving Pos. Swab
Manchester ..	I	Sauer 087860	121	119	2·26	76	62·8	63·9
Tottenham and Edmonton	I	Michigan D231	36	36	1·67	18	50·0	50·0
Wembley ..	I	,, ,,	35	35	2·03	24	68·6	68·6
Manchester ..	II	,, ,,	75	72	2·14	43	57·3	59·7
Leeds	I	Glaxo 61	112	104	1·63	67	59·8	64·4
Leeds	II	Glaxo 174	122	113	1·37	79	64·8	69·9
West Ham ..	I	Glaxo 174	121	121	1·94	44	36·4	36·4
Manchester ..	III	Michigan A236	105	104	2·00	75	71·4	72·1
Tottenham and Edmonton	II	,, ,,	54	48	1·52	23	42·6	47·9
Wembley ..	II	,, ,,	55	54	1·85	33	60·0	61·1
Totals			836	806	1·85	482	57·7	59·8

and at the same time. In Table XIV, however, the attack rates in children have been compiled for each vaccine and the corresponding attack rates in the unvaccinated children are also given. It is evident that the

TABLE XIV.—*Attack Rates in Vaccinated and Unvaccinated Groups for Each Batch of Vaccine Tested*

Vaccine	Attack Rate per 1,000 Child-months		% Attack Rate in "Home Exposures"		% Attack Rate in "Other Exposures"	
	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated
Sauer 087860 ..	2·64	6·72	22·2	85·0	15·0	32·9
Michigan D231 ..	0·97	7·04	7·3	79·5	4·6	36·7
Michigan A236 ..	0·60	6·48	8·9	90·0	3·8	34·8
Glaxo 61	2·02	6·61	30·4	90·5	8·7	40·8
Glaxo 174 ..	1·91	6·83	29·8	90·7	15·7	46·3

attack rate per 1,000 child-months of observation in the unvaccinated children for each of these vaccine groups was almost constant, varying only from 6.48 to 7.04. This was no doubt due to the fact that the incidence of pertussis in the general population, over the whole period of the investigation, was alike in each trial area and that no large epidemic occurred (see Chart). There was only slight variation also in the attack rate in the unvaccinated children exposed in the home—from 79.5% to 90.7%—and considerable uniformity was evident in the attack rate in the unvaccinated children in the "other exposures" category—from 32.9% to 46.3%.

It is justifiable, because of these similarities in the incidence of pertussis in the unvaccinated groups, to compare the prophylactic value of the different vaccines. Each vaccine gave substantial protection. It is evident that for the trial with the Sauer vaccine the ratio of the attack rate per 1,000 child-months of observation in the vaccinated to that in the unvaccinated group was 1:2.5. There was a slightly greater degree of protection with each of the two Glaxo vaccines, where the corresponding ratios were 1:3.3 and 1:3.6. The two Michigan vaccines, however, gave a considerably greater degree of protection than any of the others; the ratios with these were 1:7.3 and 1:10.8. Similar differences in the degree of protection are revealed by the rates of attack in "home exposures" and "other exposures."

Further Studies

It is evident from the results of these field trials that pertussis vaccines may vary considerably in their protective property. This variation in potency is possibly related to the many variables concerned in the preparation of vaccines, such as the selection of strains, the composition of the medium on which the organisms are grown, the method of harvesting the growth, and the nature of the killing and preservative agents. In these trials the vaccines prepared by the Michigan Department of Health proved to be more potent in the field than any of the others tested, and full details of the method of preparation have been made available to the Committee. Vaccines prepared in this country by the Michigan method are now being tested in the field in comparison with a new batch of Michigan vaccine with the object of ascertaining whether the method, in the hands of British manufacturers, gives vaccines of high potency. Some of the field trials with these new vaccines have already been begun in Manchester, Oxford, Cardiff, Poole, Leeds, Tottenham, and Wembley.

Although the Michigan method of preparation may, in the hands of others, prove to give vaccine of high prophylactic potency, it would not be advisable to adopt the method as a standard procedure, as other methods may be equally satisfactory or even better. The ideal method of controlling the prophylactic activity of pertussis vaccine would be to adopt a reference vaccine which has been shown to give substantial protection in the field and in terms of which the potency of other vaccines could be assayed by means of comparative tests made in the laboratory. Such a procedure is being investigated in the United States of America by the Biologics Control Laboratory of the National Institutes of Health and the Michigan Department of Health (Pittman and Lieberman, 1948; Kendrick *et al.*, 1947, 1949), and a provisional reference pertussis vaccine has been adopted (United States Biologics Control Laboratory, 1948).

The method of comparative testing employed by these workers necessitates the immunization of mice with pertussis vaccine and the determination of the level of immunity by the intracerebral challenge injection of virulent *H. pertussis*. It is, however, not yet known whether there is a correlation between this laboratory test and the ability of vaccines to induce immunity in children. It was therefore decided to investigate this problem by testing the prophylactic property of a number of vaccines in children and comparing the results with those obtained by laboratory tests. With this aim in view, trials were begun in Manchester, Oxford, Cardiff, Poole, Walthamstow, and Leyton, and have now been in progress for two years. The results will be reported later.

Summary and Conclusions

Controlled trials were made to assess the prophylactic value of pertussis vaccine in children. Those between the ages of 6 and 18 months whose parents consented to take part in the study were divided by the method of random sampling into two groups of equal size. The groups proved to be strikingly similar in the average age of the trial children, the average number of children in the families, and the average duration of observation. The close similarity of the groups was also evident from a comparative history of breast-feeding, infectious diseases other than pertussis, immunization against diphtheria, and vaccination against smallpox.

The children in one group (referred to as the vaccinated group) were inoculated with pertussis vaccine and those in the other (referred to as the unvaccinated group) with "anti-catarrhal" vaccine containing no *H. pertussis*. Each child was visited at frequent intervals for a period of two to three years by a nurse-investigator. Neither parents nor observers knew to which group a child had been allocated.

Five batches of pertussis vaccine from three manufacturers—Parke Davis & Co., of Detroit, the Michigan Department of Health, and Glaxo Laboratories, Ltd.—were tested. Ten separate field trials were made in five different areas. In all, 7,558 children were inoculated and followed up—3,801 in the vaccinated and 3,757 in the unvaccinated group. With only a few exceptions there were no severe local or general reactions after inoculation. None of the children had convulsions and in none did poliomyelitis develop within two months of inoculation.

In all the trials, 149 vaccinated and 687 unvaccinated children developed pertussis. The corresponding attack rates per 1,000 child-months of observation were 1.45 and 6.72, giving a reduction in the incidence of the disease of 78%. Among children exposed to pertussis in their own homes the attack rates were 18.2% in the vaccinated and 87.3% in the unvaccinated groups. The cases that occurred in the vaccinated were on the average less severe and of shorter duration than those in the unvaccinated children. During the two- to

three-year periods of observation there was no evidence of a waning in the degree of protection afforded by the pertussis vaccines.

Swabs were taken from 96.4% of all clinical cases, and in 59.8% a bacteriological confirmation was obtained.

Each batch of vaccine gave substantial protection, but the two batches supplied by the Michigan Department of Health gave a considerably greater degree of protection than the others.

Vaccines prepared in this country according to the method used by the Michigan Department of Health are now being tested in similar field trials. An investigation is also being made in which the immunizing properties of vaccines as indicated by laboratory tests are being compared with their prophylactic value in the field.

The Whooping-cough Immunization Committee and the medical officers of health concerned wish to record their gratitude to the many parents who, in the full knowledge that their children would not necessarily receive pertussis vaccine, consented to take part in the investigation. They also wish to thank Messrs. Parke Davis and Co., of Detroit, the Michigan Department of Health, and Messrs. Glaxo Laboratories Ltd. for the free supply of pertussis vaccines, and Messrs. Burroughs Wellcome and Co. for the free supply of "anticatarrhal" vaccine.

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The World Health Organization is helping the Indian Government take preventive action against possible outbreaks of cholera and malaria in the famine-stricken area of Bihar. An appropriation of $30,000 was made to purchase bleaching powder to sterilize drinking-water as a measure against cholera, and proguanil tablets to prevent malaria. In presenting the Indian request for aid, the W.H.O. regional director for South-east Asia stated that the area affected, with a population of about 20 million people, is normally subject to outbreaks of cholera and malaria, and that the famine conditions that now exist are bound to aggravate the situation.

PROGNOSIS AND TREATMENT OF CARDIAC INFARCTION

A SURVEY OF 200 PATIENTS

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The mortality in untreated series of myocardial infarction has been extensively reviewed in recent publications (Tulloch and Gilchrist, 1950; *Lancet*, 1950). The figures given in different statistics vary between 20 and 40% for the first four weeks following cardiac infarction. About 25% of the patients die either in the seizure or within two months of it, 50% by the end of the first year, 75% by the end of the third year, and 80% by the end of five years (Katz, Mills, and Cisneros, 1949). The average period of survival after the appearance of coronary artery disease, estimated at three and a half years by Levine and Rosenbaum (1941), is now said by McCain, Kline, and Gilson (1950) to be only one and a half years. Cardiac infarction is not a disease of uniform severity, and statistics, however large in number, give only a rough average of the variants encountered in cardiological practice. Although the prognostic significance of the individual symptoms was subjected to painstaking analysis by Rosenbaum and Levine (1941) and by Mintz and Katz (1947), it is rather the grouping of symptoms into clinical features which determines the degree of gravity and the outcome of the disease.

We were impressed by the fact that in a survey comprising 109 cases of cardiac infarction, mostly untreated by anticoagulants, there were 33—almost one-third—in which shock and cardiac failure were absent and in which prolonged cardiac pain accompanied by conclusive electrocardiographic changes were frequently the only diagnostic features (Papp and Shirley Smith, 1951). All these patients survived the two-months period of close observation. Post-mortem evidence has since proved that these slight coronary attacks correspond to subepicardial cardiac infarctions rarely reaching the endocardial surface. Others in our series were unmistakable examples of severe cardiac infarction showing the critical combination of persistent circulatory shock and early congestive heart failure. A middle group of moderate cases could be formed of those in which the ominous symptoms of the severe group appeared only for a short time, in which shock did not outlast the pain, and in which signs of left ventricular failure did not go beyond fleeting basal crepitations.

It seemed worth while, therefore, to investigate separately the prognosis of patients afflicted with slight, moderate, and severe infarctions; to review the complications in the different groups and the ensuing disabilities; and to correlate the clinical and electrocardiographic findings. It was hoped that this study might help to define the treatment of the individual case and lend some precision to prognosis. Patients who had full anticoagulant treatment were considered separately.

Material and Method of Study

From May, 1948, till the end of December, 1950, 200 consecutive cases of cardiac infarction (25 of them treated with anticoagulants) were collected from three different sources—from consultant practice (K. S. S.), from general practice (C.P.), and from Charing Cross Hospital in- and out-patient departments. These were partly recent cases with infarctions less than a fortnight old, and partly older ones which came for control and in which detailed data of the original attack were available. Each case was assessed on the basis of the clinical and electrocardiographic signs exhibited during the attack, and was classified as slight, moderate, or severe. The condition for inclusion in the series was that at least two conclusive electrocardiograms should show the usual serial changes seen in cardiac infarction, except in the case of patients who died within days, when one conclusive cardiogram was accepted as evidence. Patients seen in hospital and general practice came frequently under review, which included clinical, radiological, and cardiographic examinations.

At the end of December, 1950, follow-up letters were sent to the doctors of those patients who had not been seen for three months or more. The questions asked were simple and straightforward, as the many clear answers proved. The patients who were observed during repeated infarctions or who had had previous infarction were assessed for the last one. Those who could not be followed up were included in the two-months period of close observation. Each patient was seen by one of us; most patients were seen by both of us.

Overall Classification: Source, Sex Incidence, Mortality

Severe cardiac infarction formed the largest group; slight cardiac infarctions were rather fewer, and infarction of moderate grade made up the smallest group (Table I). While almost half of the severe cases were hospital in-patients admitted through the casualty department or Emergency Bed Service, less than one-third of the slight cases were so admitted. All the hospital out-patients who did not become in-patients were slight cases. Patients seen first in consultant and general practice were fairly evenly distributed in the three groups.

TABLE I.—*Source of Material*

	Hospital In-patients	Consultant Practice	General Practice	Hospital Out-patients	Total
Slight cardiac infarction ..	20	27	10	13	70
Moderate cardiac infarction ..	19	15	8	—	42
Severe cardiac infarction ..	40	32	16	—	88
Total ..	79	74	34	13	200

Table II, like Table I, comprises the whole series, whether treated or untreated by anticoagulants, and shows the age and sex incidence and total mortality. It furnishes a solid basis for this investigation, for the all-round mortality of the series is 25%. While the mortality of the slight group is only 8.6%, that of the moderate group is 11.9% and that of the severe group 44.3%.

The sex ratio confirmed the well-known preponderance of men over women (4.9 : 1), though the mortality was about equal—24.7% in men and 26% in women. There was, however, considerable difference in the separate groups: no woman died of slight or moderate cardiac infarction; but in the group of severe cardiac infarction 9 out of 17 women died, whereas 30 out of 71 men died. Thus in severe cardiac infarction, mortality seems to be higher in women (53%) than in men (42%).

TABLE II.—*Age and Sex Incidence. Mortality*

		30–39		40–49		50–59		60–69		70–79		Total	
		M	F	M	F	M	F	M	F	M	F	M	F
Slight cardiac infarction (70 cases)	Alive	2	—	13	—	20	3	17	7	2	—	54	10
	Dead	—	—	2	—	2	—	1	—	1	—	6	—
Moderate cardiac infarction (42 cases)	Alive	2	—	6	—	11	1	9	3	2	3	30	7
	Dead	—	—	—	—	1	—	4	—	—	—	5	—
Severe cardiac infarction (88 cases	Alive	—	—	8	—	19	4	11	4	3	—	41	8
	Dead	—	—	3	—	8	3	14	6	5	—	30	9
Total												166	34

Proportion of men to women, 4·9 : 1. Total mortality, 25%. Mortality of slight cardiac infarction, 8·6%. Mortality of moderate cardiac infarction, 11·9%. Mortality of severe cardiac infarction, 44·3%.

TABLE III.—*Symptoms of Cardiac Infarction*

	Predisposing Conditions	Pre-existent Cardiac Enl.		Previous Infarction	Angina	Infarction Pain Absent	Infarction Pain Present	One Inj. of Mo	Rep. Inj. of Mo	Circulatory Shock		Pulmonary Congestion	Early C.H.F.	Arrhythmia	Pyrexia	E.S.R. 20 mm.+ W.B.C. 9,000+	Electrocardiogram						
		No C.H.F.	C.H.F.							Sl.	Sev.						Ant.	A.w B.B.B. or H.B.	A/L	P.	P.w B.B.B. or H.B.	P/L	A/P
Slight cardiac infarction (70 cases)	33	11	—	6	47	17	53	13	1	11	—	1	—	2	9	5	40	1	13	13	—	3	—
Moderate cardiac infarction (42 cases)	17	3	—	8	21	—	42	21	7	15	2	10	1	4	21	17	22	2	5	9	—	4	—
Severe cardiac infarction (88 cases)	36	15	17	25	44	10	78	43	32	17	51	48	39	21	53	36	31	6	8	18	11	7	7

Enl. = Enlargement; C.H.F. = Congestive heart failure; Mo = morphine; Rep. = Repeated; Sl. = Slight; Sev. = Severe; A. = Anterior; A/L = Antero-lateral; P. = Posterior infarction; P/L = Postero-lateral infarction; A/P = Antero-posterior infarction; B.B.B. = Bundle-branch block; H.B. = Heart-block.

Prognosis of Untreated Slight Cardiac Infarction

Included in the 69 patients of this group are the 33 cases published as "slight coronary attack" (Papp and Shirley Smith, 1951) which are recognized as slight cardiac infarctions. Cardiac pain in slight cardiac infarction may be long-lasting (up to 12 hours) when it is intermittent, but is less severe than in the moderate or severe group; only 13 asked for relief by injection, and a second injection of morphine was necessary in only one case (Table III). As in the other groups, angina of effort preceded cardiac infarction for months or years in 47 patients, and in 17 of these prolonged infarction pain was absent (Morgan Jones and Wade, 1949; Stein, 1950). Diagnosis here was based on the electrocardiogram only.

Slight shock was observed in 11 and was responsible for lowering of the systolic blood pressure for a short time to 100–110; even in these patients the pulse pressure never fell under 30 mm., while in the others the fall of the blood pressure was irrelevant. Pyrexia for a few days was known to be present in nine, but many patients were seen late. Out of 20 who were seen early enough a raised E.S.R. or white-cell count was present in five. Basal crepitations were found in one for a short time, but none showed congestive heart failure. The ectopic rhythm present during the attack in two disappeared without treatment as soon as the pain subsided. The electrocardiographic location of the ischaemic zone was more often anterior and antero-lateral than posterior. The presence of bundle-branch block or complete heart-block was exceptional; in the only patient in whom right bundle-branch block was found this probably existed before the actual infarction.

No patient out of these 69 died during the two months of close observation, in which the overall mortality rate is said to be 20–40% (Table IV); moreover, none had further infarction or developed congestive heart failure during this time. Cerebral embolism was observed in Case 7, eight months after slight cardiac infarction; he recovered with no disability. Multiple pulmonary infarcts were found on post-mortem examination in Case 155; these were not due to embolism but to severe pulmonary arteriosclerosis. This, in association with coronary arteriosclerosis, was responsible for the congestive heart failure of which he died. On post-mortem examination fibrotic scars were found in the two predicted myocardial areas—one postero-basal, the other antero-septal where the electrocardiogram had shown acute ischaemia three and a half years and one year previously after slight cardiac infarctions. Case 197 died in pulmonary oedema, Cases 187 and 162 died one and one and a half years later of further cardiac infarction, and Case 179, aged 72, died suddenly two years later of probable ventricular fibrillation. Case 188 died in unknown circumstances.

Though 45 patients were active, 35 out of 63 who were alive continued having angina of effort; in nine it was so severe that they were disabled by it. One of these had to be subjected to stellate ganglionectomy four years later.

Predisposing conditions include hypertension, diabetes, obesity, intermittent claudication, and chain smoking. No particularly adverse prognostic significance could be attached to any of these factors singly or in combination, for they were present in similar proportion in the moderate and severe groups. Precipitating causes (Master, 1946) are not listed, for they were rarely instrumental in provoking infarction. Pre-existent cardiac enlargement was slight in all, and mostly was of hypertensive origin. Except in Case 155, slight cardiac infarction did not produce or make worse existing cardiac enlargement. The electrocardiographic changes were described elsewhere; they are of diagnostic but not of prognostic significance. The far-reaching cardiographic restoration in almost two-thirds of the patients is possible because the Q waves of through-and-through infarction are commonly absent. Though the general impression is that fewer of those who made electrocardiographic recovery were disabled by angina, the exceptions are too many for this to be of prognostic value.

TABLE IV.—*Prognosis of Untreated Slight Cardiac Infarction (69 Cases)*

Last Follow-up (Years):	½	½	1	1½	2	2½	3	3½	4	4½	5	Total
No. of cases	13	10	10	6	9	10	2	4	2	2	1	69
Angina: Mild	6	3	4	2	3	2	—	1	—	2	—	23
Angina: Moderate	1	3	2	—	1	—	1		1	—	—	9
Angina: Severe	1	1	—	—	1	3	1	1	—	—	—	8
Further infarction	—	—	2	1	1	—	—	—	1	—	—	5
Congestive heart failure	—	—	—	—	—	—	—	1	—	—	—	1
Thrombo-embolic complications	—	1	—	—	—	—	—	1	—	—	—	2
No complaints	5	2	3	2	3	4	—	1	1	—	1	22
Active	6	7	8	4	5	8	—	2	2	2	1	45
Incapacitated	2	2	1	—	2	2	1	1	—	—	—	11
Died	—	1	1	2	1	—	—	1	—	—	—	6
E.C.: Unchanged	7	3	3	2	2	4	—	1	—	1	—	23
E.C.: Improved	6	4	2	4	4	2	1	3	—	—	—	26
E.C.: Recovered	—	2	3	—	2	3	1	—	2	1	1	15
E.C.: Worse	—	1	2	—	1	1	—	—	—	—	—	5

Prognosis of Untreated Moderate Cardiac Infarction

This is the smallest of the three groups, with 39 patients; as it is the intermediate one, some overlapping is inevitable with both slight and severe cardiac infarction. These patients, though not critically ill, showed for a short time some of the signs found in severe cardiac infarction (Table III). Infarction pain was present in all, and 28 were in need of morphine, 7 of repeated injections. The incidence of circulatory shock was higher (17) and shock was severe in two, one of whom also developed signs of early congestive heart failure. Pulmonary congestion was present in 10 and was transitory in all except one. Pyrexia and increase in white-cell count and E.S.R. were present in greater proportion than in the previous group.

Two patients died during the first two months and four developed thrombo-embolic complications. Five had further cardiac infarctions, and in four congestive heart failure appeared in contrast to one in the slight group. Cardiac infarction, thrombo-embolic complications, and congestive heart failure, singly or in combination, were the causes of death in three cases in the

TABLE V.—*Prognosis of Untreated Moderate Cardiac Infarction (39 Cases)*

Last Follow-up (Years):	½	½	1	1½	2	2½	3	3½	4	4½	7–8	Total
No. of cases	7	5	5	7	2	1	3	3	2	2	2	39
Angina: Mild	—	1	2	—	—	—	1	2	1	2	—	9
Angina: Moderate	2	1	—	3	—	—	—	—	—	—	—	6
Angina: Severe	—	1	1	—	—	—	1	—	—	—	1	4
Further infarction	1	—	—	—	1	—	1	1	—	1	—	5
Congestive heart failure	—	1	—	—	2	1	—	—	—	—	—	4
Thrombo-embolic complications	1	—	—	1	—	—	—	1	1	—	—	4
No complaints	3	2	2	4	—	—	1	—	1	—	1	14
Active	3	4	3	6	—	—	2	2	2	1	2	25
Incapacitated	1	1	1	—	—	1	1	—	—	1	—	6
Died	2	—	—	—	2	—	—	1	—	—	—	5
E.C.: Unchanged	4	3	2	3	1	—	1	1	1	1	—	17
E.C.: Improved	2	2	3	4	—	1	1	1	1	—	2	17
E.C.: Worse	1	—	—	—	1	—	1	1	—	1	—	5

late follow-up series (Table V). The proportion of angina is similar to that in the previous group, but it was mostly slight and produced incapacity in two only. No electrocardiogram reverted to normal, though in less than half the signs of actual infarction have disappeared. Thus the immediate prognosis in this group is not much worse than in the previous one, though the clinical and electrocardiographic signs are more severe.

Prognosis of Untreated Severe Cardiac Infarction

The dominant and grave symptom (Table III) was circulatory shock, which was present in 68 of the 88 patients in the severe group; it was mostly severe and outlasted the pain by hours or days. Basal congestion developed in more than half and progressed often to basal consolidation, which prolonged the period of pyrexia and was partly responsible for the high white-cell count and E.S.R. in 36. Shock when severe prevents the development of pyrexia. More than one-third of the patients had pre-existent cardiac enlargement due to either hypertensive or ischaemic heart disease, and half of these were in failure when they developed recent cardiac infarction. The earliest signs of congestive heart failure after severe cardiac infarction were high pulse rate, gallop rhythm, and pulmonary congestion.

Out of 39 who showed early signs of left ventricular failure 21 died within two months and a further 12 within three years (Table VI). The longest survival period among the five who are still alive is three and a half years. Those who in addition to early left ventricular failure developed right ventricular failure died within weeks or months; a similar experience was recorded also by Selzer (1948). An exception was Case 140, in whom subtotal thyroidectomy was performed during irreducible right heart failure, six months after the second cardiac infarction. He is alive and active after three years. The combination of circulatory shock and congestive heart failure was particularly critical. Cardiac infarction was silent in five cases in which it arose during gross congestive heart failure; the pain-equivalent here was paroxysmal dyspnoea.

Persistent arrhythmia, whether auricular fibrillation, flutter, ectopic rhythms, or salvos of ventricular extrasystoles, is of serious prognostic significance, and no patient who developed persistent auricular fibrillation during the acute stage survived. In our experience the electrocardiographic location of the ischaemic area was diagnostic of severe infarction only when the record showed antero-posterior infarction (Roesler and Dressler, 1947) or when posterior infarction was associated with bundle-branch block or heart-block (Table III). The latter, if transitory, may not be of grave significance; all five patients in whom it ushered in cardiac infarction but disappeared after few hours or days survived the two-months period, and three are known to be still alive. The infarction was "silent" in them and syncope was here the pain-equivalent (Papp, 1951).

Severe cardiac infarction leaves indelible traces in the electrocardiogram. In only 3 out of 67 did the signs of actual infarction disappear, but even in these the record remained abnormal (Table VI). The fact that 50% of these patients had congestive heart failure is in agreement with the findings of Mills *et al.* (1949), who also emphasized the frequency of congestive heart failure in those whose electrocardiogram showed gross persistent changes.

Of the 67 patients with untreated severe cardiac infarction 33 died. Two-thirds of the deaths occurred during the first two months and the remaining one-third during the succeeding three years. The disability in 9 out of 34 who survived was due more to congestive heart failure than to angina; in fact, only three were disabled by severe angina, and this is in contrast with the slight and moderate group. Eight were free from complaints though two had cardiac aneurysm. Twenty-two were able to resume normal activity, mostly in sedentary ocupations.

TABLE VI.—*Prognosis of Untreated Severe Cardiac Infarction (67 Cases)*

Last Follow-up (Years):	½	½	1	1½	2	2½	3	3½	4	Total
No. of cases	28	5	5	7	7	6	5	3	1	67
Angina: Mild	1	—	1	3	2	3	1	—	—	11
Angina: Moderate	—	—	—	1	—	—	—	—	1	2
Angina: Severe	1	1	—	—	—	1	—	—	—	3
Further infarction	10	1	1	3	1	1	1	—	1	19
Cardiac aneurysm	—	1	—	—	—	—	1	—	—	2
Cardiac enlargement	23	3	3	4	2	3	2	1	—	41
Congestive heart failure	21	1	1	4	2	2	1	1	—	33
Thrombo-embolic complications	6	1	—	—	1	—	2	—	—	10
No complaints	2	—	2	—	1	1	1	1	—	8
Active	1	1	3	4	4	4	3	2	—	22
Incapacitated	5	1	—	—	1	1	—	—	1	9
Died	21	3	2	3	2	1	1	—	—	33
E.C.: Signs of infarction	27	5	5	7	7	5	5	2	1	64
E.C.: No signs of infarction	1	—	—	—	—	1	—	1	—	3

Treated Series

One slight, three moderate, and 21 severe cases of cardiac infarction are included in this series (Table VII). Many more were treated, but only those were selected

TABLE VII.—*Result of Anticoagulant Treatment in 25 Cases of Cardiac Infarction (1 Slight, 3 Moderate, 21 Severe)*

	During Treatment	Last Follow-up (Years) of 21 Patients Alive at End of Treatment					
		¼	½	1	1½	2½	3
No. of cases ..	25	3	6	4	5	2	1
Recurrent cardiac pain or angina ..	4	—	1	3	3	—	—
Further infarction	3	1	—	1	—	—	—
Thrombo-embolism	2	—	—	1	—	—	—
Haemorrhage ..	5	—	—	—	—	—	—
Cardiac failure ..	10	1	2	—	—	—	1
Cardiac aneurysm ..	—	—	—	1	—	—	—
No complaints ..	11	2	3	1	3	2	1
Active	—	1	2	2	4	1	1
Incapacitated ..	—	—	1	1	—	—	—
Died	4	1	1	—	—	—	—
E.C. Signs of infarction ..	25	3	5	4	4	2	1
E.C. No signs of infarction	—	—	1	—	1	—	—

in whom treatment was continued for longer than a fortnight, in whom satisfactory prothrombin levels were obtained, and in whom treatment was started within four or five days after infarction. Some were treated with heparin and dicoumarol after the method of Wright, Marple, and Beck (1948), others with heparin alone, and others with "tromexan." When laboratory facilities were not available heparin was preferred. The reason for treatment in the slight and moderate cases was persistence of cardiac pain.

The four patients with slight and moderate infarction are alive; out of the 21 severe cases only four died during the period of treatment (Table VII). Death was due to cardiac failure in all, and so was it in a further two who died within two and six months after infarction. Thrombo-embolism occurred in two during treatment; both had pulmonary infarctions, but these were not severe. Both survived, while in the untreated severe group thrombo-embolism occurred in seven during the first three months (peripheral and cerebral in four, pulmonary in three) and was the cause of death in three. Further cardiac infarction was observed in three; in two it occurred before satisfactory prothrombin levels were reached; this also compares favourably with the untreated series. The influence on recurrent cardiac pain after infarction was variable, and the two patients, one of the slight and another of the moderate group, had to be subjected to stellate ganglionectomy a few months later. In five patients haemorrhagic complications occurred and treatment had to be stopped in three after the second week. In another three, these complications occurred during the first few days and treatment had to be abandoned; these cases were regarded as untreated and are not included in this series.

The late follow-up has shown no difference from the untreated series. The absence of severe angina was remarkable, but this only confirms what has been noted in the untreated series of severe cardiac infarction.

Circumstances and Cause of Death (50 Cases)

These were similar in the 6 slight, 5 moderate, and 39 severe cases of cardiac infarction, whether treated or untreated. Post-mortem confirmation was obtained in 11 instances. Sudden death in cardiac pain may occur at any time after infarction and is possibly due to further infarction or to massive embolism (seven cases). Cardiac rupture may also cause a fatal termination in the first few days (Gans, 1951). Sudden death in unexplained circumstances (two during sleep, two on the road, one on the bedpan) may be due to the causes mentioned (in one instance post-mortem examination showed a recent cardiac infarction). Death in shock and cardiac pain occurred in three cases within hours or days after the beginning of infarction, while most of the nine who also showed signs of congestive heart failure died between the first and fourth weeks.

Congestive heart failure caused death usually at a later stage (18 cases), and was twice associated with pulmonary infarction. Pulmonary infarction was in neither instance due to embolism but to local thrombosis. Peripheral and cerebral embolism were fatal complications in five patients, but in only one was post-mortem confirmation obtained. In two further cases the clinical diagnosis was not substantiated at necropsy: although myocardial infarction with mural thrombosis was found on post-mortem examination, the limb symptoms were due to arteriosclerotic gangrene precipitated by circulatory shock and possibly vasoconstriction (Swan and Henderson, 1951). Unrelated conditions included bronchopneumonia and suicide. In each instance there was post-mortem confirmation of healed cardiac infarction. One patient died in unknown circumstances.

Death in 90% was due to further cardiac infarction, shock, or congestive heart failure. In only 10% could thrombo-embolism be held responsible, and then it was more often due to local thrombosis than to embolic phenomena.

Repeated Cardiac Infarction

More than half of the deaths occurred during or following a first attack of cardiac infarction. Twelve patients died after the second episode, the date of the first cardiac infarction being known in 10. The survival periods from the first attack were two months in one, from one to three years in six, and from seven to eight years in two. In five who succumbed after the third cardiac infarction the survival periods were five months in one, six to seven years in two, and 12 years in two. Follow-up of surviving patients showed comparable results: out of 20 who had repeated attacks, five could be followed up to two years, nine up to four years, five up to seven years, and one up to 20 years after the first attack.

It is not the number of cardiac infarctions but the severity of the single attacks which is of prognostic significance. Patients who had previous infarctions might develop successively small marginal ischaemic areas; the clinical expression of such slow extension of infarction was a recurrence of slight or moderate attacks of cardiac infarction. What is being accomplished in severe cardiac infarction in one stage may be accomplished gradually by repeated cardiac infarctions. Finally, a stage may be reached when the patient is without symptoms or disability for a long time; such a course corresponds to the case of severe cardiac infarction in which suddenly a large coronary artery is occluded. Electrocardiography here is of great prognostic value, as a second infarction in a hitherto unaffected area is of grave significance.

Treatment

The technique of anticoagulant treatment is well known (Wright, 1950). Heparin is given either by intravenous injection through a polythene tube, 5,000–7,500 units four-hourly, or by intramuscular injection 15,000–25,000 units twice a day. The latter method is obviously

to be preferred in general practice; it does not need much laboratory control, and the addition of 1 ml. of 1% procaine makes the injection almost painless (Abrahams, 1950). The cost and the risk of haematoma formation at the place of the injections are its great drawbacks. If laboratory control is available dicoumarol should be given with heparin; if the initial prothrombin time is normal (12–18 seconds) 300 mg. should be given in divided doses the first day, 200 mg. the second day, and 100 mg. the third day. After 48 hours heparin can be discontinued, as a satisfactory prothrombin time will be reached by then. This is 25–40 seconds, with a control around 15–20 seconds, and the aim is to keep the patient on this level during the three to four weeks' treatment. The average maintenance dose of dicoumarol is 50–100 mg. daily; but it can be higher or lower, and has to be worked out for every patient.

Tromexan is safer than dicoumarol since it has no lag action, and the prothrombin time returns to normal within 24 hours, should complications make its discontinuance necessary. Furthermore, a satisfactory prothrombin time can be reached within 24 hours and therefore the addition of heparin may not be necessary. The dose is 1,200 mg. the first day, 900 mg. the second day, 600 mg. the third day. The maintenance dose is 150–600 mg.; in our experience a stable prothrombin time is more difficult to obtain with tromexan than with dicoumarol. About 75–80% of the patients can be stabilized on a satisfactory prothrombin level, and, in these, thrice-weekly prothrombin estimations during the first fortnight and twice weekly thereafter will suffice. The rest of the patients are unstable reactors in whom the prothrombin time shows wide variations; in spite of daily laboratory control they may develop haemorrhagic complications, and should be referred to hospital or treated with heparin.

A daily examination of the patients for subcutaneous or oral haematomas, and the inspection of every urine specimen for haematuria, are essential, as haemorrhages may affect vital regions and be difficult to control. If they occur in patients on heparin, 5–10 ml. of protamine sulphate should be injected intravenously and treatment be discontinued until the clotting time becomes normal (4–7 minutes). Treatment thereafter should be continued under laboratory control and heparin should be temporarily discontinued if the clotting time exceeds 20 minutes. If the patient is being treated with tromexan or dicoumarol a prothrombin time of 50 seconds (with a control time of 15–20 seconds) is the danger signal. If the patient is on tromexan, its discontinuance for one day will lower the prothrombin time to near or below the maintenance level; if on dicoumarol, 60–70 mg. of vitamin K intravenously, followed by a second dose four hours later, may avert haemorrhage. In the presence of haemorrhage repeated transfusions with fresh whole blood may be necessary.

In general practice choice of the drug depends on the laboratory control available. With reasonable laboratory control tromexan is safer than dicoumarol. With no laboratory control intramuscular heparin is the only alternative, though it is much more unpleasant for the patient and not altogether devoid of danger. Hepatic or renal disease, ulcerated surfaces, pregnancy, and haemorrhagic tendency are absolute contraindications for both.

Additional treatment includes penicillin, digitalis, quinidine, oxygen, and analgesics. If pyrexia persists for more than three to four days it is commonly due to infection of the congested lung bases, and penicillin treatment should not be delayed. Cardiac failure is better treated with intramuscular ouabaine injections (0.25–0.5 mg. daily) than with digitalis, though in the presence of shock the effect of both is unsatisfactory. Extrasystolic arrhythmia requires quinidine, 5 gr. (0.32 g.) three or four times a day, to reduce the danger of ventricular fibrillation. An oxygen tent may be life-saving when shock persists or when cyanosis and engorgement of the neck veins indicate right-sided heart failure. Recurrent cardiac pain should be treated with morphine if severe; if it is moderate, "nepenthe," 20 min. (1.2 ml.), or pethidine, 100 mg. by injection or by mouth, may suffice and have less unpleasant side-effects. Sedation by "sodium amytal," 2 gr. (0.13 g.) three times a day, is less depressing than by phenobarbitone.

Absolute rest in bed should be continued for four to six weeks in severe cardiac infarction; if failure exists after this period nothing is gained by prolonging the complete rest. The patient should be treated as a cardiac invalid and be allowed the amount of exercise compatible with his reduced cardiac reserve. In contrast, in slight and moderate cardiac infarction complete immobility in bed is not only unnecessary but may be harmful. To prevent pulmonary congestion and phlebothrombosis these patients should have respiratory exercises, should move their legs, and should be allowed to use the commode as soon as pyrexia has subsided. After two to three weeks they are allowed up by gradual stages provided the E.S.R. has become normal.

Discussion

The results of this investigation confirm the statement made by many others that anticoagulant treatment considerably reduces the mortality of cardiac infarction. Thus the suggestion that it should be used in all cases of coronary thrombosis (Wright *et al.*, 1948) and that it "should be considered for every sufferer of myocardial infarction" (Tulloch and Gilchrist, 1950) is based on good evidence. Furthermore, preventive treatment of impending cardiac infarction has been advocated by Wood (1950) in patients who have prolonged attacks of angina at rest; to these cases can be added patients who have increasingly severe angina of effort of less than a fortnight's duration, for in our experience many of these have either already sustained cardiac infarction or are in danger of it. The limitation of hospital accommodation, the non-existent laboratory facilities in general practice, and the cost of intramuscular heparin treatment as advocated by Abrahams (1950) (about £60–£70 for three to four weeks) make a selection of cases imperative.

Our investigations have shown that the mortality of untreated cases of slight and moderate cardiac infarction during the first two months of close observation is less than 2% (Tables IV and V) and that the incidence of thrombo-embolic complications is negligible. Thus over half of the patients with cardiac infarction seen in general, consultant, and hospital practice will be at no disadvantage through having conservative treatment. In moderate cardiac infarction, where the clinical symptoms may be equivocal, the electrocardiographic signs may tilt the balance for or against anticoagulant treatment, while the risks attending the use of anticoagulants have to be remembered.

There is the same gradation in severity in cardiac infarction as there is from angina to cardiac infarction

(Freedberg *et al.*, 1948); in fact, there is no strict dividing-line between these two conditions, which are differentiated more for didactic than for pathological reasons. The first attack of angina may be the clinical expression of cardiac infarction and, conversely, severe coronary arteriosclerosis may be symptomless until it produces fatal cardiac infarction (Cassidy, 1946). The successive evolution of slight and moderate cardiac infarction is often similar to ordinary angina of effort, and in fact many of these patients are severely disabled by angina though their electrocardiogram may have reverted to normal.

Slight cardiac infarction may be only an episode in the clinical history of slowly progressing coronary narrowing which favours development of collateral circulation (Blumgart *et al.*, 1950). In contrast, the sudden occlusion of a large coronary artery in a heart previously unprepared by the development of collateral circulation produces severe cardiac damage; but once the patient is over the critical period and does not develop congestive heart failure, he may eventually become able to lead a comparatively normal life. These are only the two extreme types of the disease, and their combination is frequent. Nevertheless they justify a variation of therapeutic approach to cardiac infarction according to the severity, even when the symptoms in the individual patient vary if long enough observed (Boas, 1951).

The diagnosis of severe cardiac infarction can nearly always be made within 24 hours. Prolonged continuous pain requiring repeated injections of morphine is the first sign; if circulatory shock is delayed, a mounting pulse rate and a falling pulse pressure (25 mm. or under) herald its approach. All the other signs which make up the clinical picture of severe myocardial infarction are the secondary effects of circulatory shock associated later with left ventricular failure. They are in order of appearance basal crepitations, increase of the pulse rate, and gallop rhythm.

The influence of circulatory shock on the myocardium favours cardiac failure by extension of the infarcted area (Corday *et al.*, 1949); left ventricular failure increases circulatory embarrassment in the lungs and may cause pulmonary oedema or pulmonary consolidation, or both. Thus pulmonary infarction during the first few days following cardiac infarction is only exceptionally of embolic origin, as infarction of the right ventricular wall, and therefore formation of mural thrombosis in the right ventricle, is rare. If shock of cardiac origin could be effectively treated, anticoagulant treatment would be of secondary importance. As the results of treatment of shock are uncertain (Schwartz, 1947; Corday *et al.*, 1949; Epstein and Relman, 1949) one aims to reduce the thrombogenic effect of slowing of the circulation (Macfarlane, 1950) by prolonging the clotting-time (heparin) or by reducing the prothrombin level (coumarin drugs) of the blood.

In our experience real embolic complications amount to no more than 15% (Shirley Smith, 1950); thrombo-embolic complications or peripheral ischaemia may occur so soon after cardiac infarction that they cannot be prevented in spite of effective anticoagulant treatment. The risk of phlebothrombosis of the legs—the embolic source of pulmonary infarction—can be reduced by anticoagulant treatment though not abolished.

In about 15% of cases increasingly severe premonitory pain may herald the infarction for days or weeks, the electrocardiogram remaining unchanged until finally the infarction develops. These cases therefore begin as myocardial ischaemia and develop into slight cardiac infarctions; yet they may progress into severe ones. The aim, then, is the prevention of impending cardiac infarction, and results in these cases are being published separately (Shirley Smith and Papp, 1951).

Summary

Two hundred consecutive cases of cardiac infarction, 175 treated on conservative lines and 25 treated with anticoagulants, were collected from consultant, general, and hospital practice and divided into three groups—slight, moderate, and severe. The prognostic significance of each of these groups was investigated separately and the clinical and electrocardiographic findings were correlated. The ages of the patients ranged from 34 to 75 years, the sex ratio was five men to one woman; the total mortality was 25%, being about equal in the sexes.

All the 69 patients with untreated slight cardiac infarction were alive at the end of two months; six men died six months to four years later (8.6%), but there were no deaths among the women. Disability for the patients' usual occupation was due to angina in 11 cases; only one had congestive heart failure three and a half years later. Normal activity was resumed in 45. Cardiographic restoration occurred in almost two-thirds of the patients irrespective of the presence of angina.

Out of 39 untreated cases of moderate cardiac infarction two died during the first two months and a further three two to three years later (12.8%). No female patient died. Four had thrombo-embolism, but only one had it during the first two months. Five had further cardiac infarction. Incapacity in four was due to congestive heart failure, in two to angina. Normal activity was resumed in 25. No cardiogram reverted to normal, though in 17 the signs of infarction have disappeared.

Out of 67 patients with untreated severe cardiac infarction 33 died (50%); two-thirds of the deaths occurred during the first two months, and the mortality in women was higher than in men. Congestive heart failure, present in 33 cases, appeared early in 21. Further infarction took place in 19, in 10 of these within two months; thrombo-embolism occurred in 10, in six of these within two months. Out of 34 who survived nine were incapacitated, mostly by congestive heart failure. Normal activity in sedentary occupation was resumed in 22. The cardiogram remained abnormal in all, and signs of infarction persisted in 64.

Twenty-five cases (1 slight, 3 moderate, and 21 severe) were treated with anticoagulants. Only four out of the 21 with severe infarction died during the first month, and two a few months later (21.6%). Thrombo-embolism was seen in only two while under treatment, and both recovered. Early cardiac failure was observed in 10, of whom six recovered. The value of anticoagulant treatment in severe cardiac infarction is confirmed. In contrast, this treatment is unnecessary in slight and moderate cardiac infarction, where the early mortality is less than 2%. In such patients, who are fundamentally sufferers from angina, cardiac infarction may be no more than an episode which does not produce permanent cardiac damage.

More than half of the deaths occurred during or following first cardiac infarction. Death in 45 (90% of the 50 who died) was due to further cardiac infarction, shock, or congestive heart failure; only in five was thrombo-embolism the cause, and then local thrombosis was more often responsible than embolism. The success of anticoagulant treatment is therefore due much less to prevention of embolism than to reduction of the thrombogenic effect of circulatory shock on the myocardium, lungs, and peripheral circulation.

The choice of anticoagulant depends on the ready availability of laboratory control. The indications for additional treatment with penicillin, ouabaine, quinidine, oxygen, and analgesics are discussed.

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ISOLATION OF SALMONELLAE FROM FAECES OF DOMESTIC ANIMALS

BY

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The importance of salmonellae as causes of disease in man and animals is recognized. Most outbreaks of food-poisoning in man caused by these organisms are thought to follow the consumption of food directly or indirectly associated with infection of animals (Topley and Wilson, 1946). Salmonella infection among domestic animals is also of economic importance to the agricultural industry and is associated with serious disease problems, particularly among young animals.

A considerable amount of evidence has accumulated from studies of clinical salmonella infection to indicate the species most commonly affected and the types of salmonellae that have been isolated from them. Less time has been devoted to the study of animals that are latently infected with salmonellae. The work carried out on this subject has been confined mainly to the examination of such material as mesenteric lymph nodes. Since the bacteria in these nodes may be constantly confined to them, this potential source of food-poisoning would be removed with the viscera after slaughter. Of more importance from the public health and agricultural points of view are animals that are symptomless faecal excreters of salmonellae. During their life such animals may give rise to disease in susceptible animals and may contaminate milk, eggs, and other food products, and after slaughter their carcasses and those of other animals may become contaminated with salmonellae.

The purpose of this paper is to report on the isolation of salmonellae from the faeces of cattle, sheep, horses, pigs, goats, chickens, turkeys, ducks, and geese. Faecal specimens were examined from adult healthy commercial stock, from animals suffering from diseases other than primary salmonella infection, and, where possible, from animals exhibited at agricultural shows. The third group was included in order to determine the effect of hygiene and general management on the incidence of salmonellae in the faeces of healthy animals.

Techniques

Several methods of isolation and preliminary identification of salmonellae from faecal specimens were tested. The method finally adopted was as follows.

A sample of faeces about the size of a hazel nut was inoculated into selenite F medium (Leifson, 1936) and into tetrathionate broth* (Rolfe, 1946). These enrichment media were incubated at 37° C. for 18 to 24 hours and plated on to Hynes's (1942) modification of Leifson's desoxycholate–citrate agar with the addition of 1% sucrose and 1% salicin (D.C.S.S.) as described by Haines, Elliot, and Tomlinson (1947). Tetrathionate broth was always used within three days of its preparation. The inoculated D.C.S.S. plates were incubated at 37° C. for 48 hours. The plates were then inspected and suspicious non-fermenting colonies were marked and tested for indole and urease production by the rapid test described by Williams Smith and Chave (1949).

Colonies negative to this test were then streaked on to a modification of the D.C.S.S. medium, the sucrose, salicin, and lactose being replaced by 1% dulcitol (D.C.D.). The plates were incubated for 24 hours at 37° C. One plate of this medium was sufficient for six to eight strains. The object of this procedure was to obtain pure cultures for further examination and to ascertain whether the cultures fermented dulcitol. Colonies on the D.C.D. medium that either fermented dulcitol and/or agglutinated with polyvalent O serum were transferred into plain Craigie tubes to induce motility and then subcultured on to moist agar slopes. The resulting cultures were studied serologically by means of antisera obtained either from the Standards Laboratory, London, or were prepared by one of us (A. B.). Organisms giving positive slide-agglutination reactions were submitted to a full tube test and their biochemical characteristics were also determined. Where necessary, final identification of cultures were made at the Salmonella Reference Laboratory, Colindale.

In the early part of the work specimens were plated directly on to D.C.S.S. medium as well as being inoculated into enrichment media. The results showed that there was no advantage from direct plating, and, because of the extra labour involved, it was discontinued. When a salmonella was isolated by one or both of the enrichment methods the original faecal specimen was plated direct on to D.C.S.S. medium. Sometimes the initial examination of suspicious colonies for indole and urease production was replaced by slide-agglutination tests with polyvalent O serum. When this was done the

*Medium A with brilliant green omitted.

colonies on the D.C.D. plates were always tested for indole and urease production before proceeding to further identification.

Results

Horses

Healthy Horses.—The total number of faecal specimens examined from healthy horses was 500. These were obtained from horses that were killed for human consumption in a large slaughterhouse in Cambridgeshire which received animals from many parts of the country. Of the 500 specimens examined, one (0.2%) was found to contain salmonellae. This culture was identified as *Salm. thompson* and was isolated after enrichment in selenite medium and in tetrathionate broth. Direct plating of this sample gave a negative result.

Diseased Horses.—Faecal specimens from horses suffering from a variety of diseases other than primary salmonella infection were received from a number of veterinary diagnostic laboratories located in various parts of the country. Two (0.4%) of the 500 faecal specimens that were examined contained salmonellae. The cultures were isolated by both enrichment media, but not by direct plating on D.C.S.S. medium. The two cultures were identified as *Salm. thompson* and *Salm. dublin.*

Cattle

Healthy Cattle.—Most of the 750 specimens from normal cattle were obtained through the help of the veterinary staff of the Animal Health Division of the Ministry of Agriculture. Only one faecal specimen was taken from any one healthy milking cow in each herd. The remaining specimens, 150 in all, were obtained from adult cattle entering a large abattoir in London. Of the 750 specimens that were examined, three (0.4%) were found to contain salmonellae. The organisms were all *Salm. dublin.* All three were isolated after enrichment in selenite. Two were also isolated after tetrathionate enrichment and by direct plating on D.C.S.S. medium.

Diseased Cattle.—Specimens from diseased cattle were received from a number of veterinary diagnostic laboratories. The diseases from which these cattle were suffering, or had died, were considered to be fairly representative of the disease conditions that affect cattle in this country ; none of them were suffering from primary salmonella infection. Salmonellae were isolated from three (0.6%) of the 500 specimens examined. The three cultures were identified as *Salm. dublin* and were isolated after enrichment in selenite media. Two of them were also isolated following enrichment in tetrathionate broth. Direct plating on D.C.S.S. medium gave negative results.

Show Cattle.—None of the faecal specimens collected from 430 cows attending the Dairy Show and the Fat Stock Show in London in 1949 were found to contain salmonellae.

Pigs

Healthy Pigs.—Faecal specimens from 600 healthy pigs were obtained through the help of the veterinary staff at two large abattoirs where large numbers of pigs are slaughtered. One abattoir was situated in the East Midlands and the other in the West Midlands. The specimens were collected over a period of a few months, so that they were representative of the pigs entering these abattoirs. Salmonellae were isolated from the faeces of four (0.67%) of the 600 pigs. The organisms were *Salm. meleagridis* (3) and *Salm. typhi-murium.* All four cultures were isolated after enrichment in selenite medium. One strain of *Salm. meleagridis* and the *Salm. typhi-murium* strain were also isolated by means of tetrathionate broth. Direct plating of the four positive specimens on D.C.S.S. medium gave negative results in all cases.

Diseased Pigs.—Owing to unavoidable circumstances it was possible to examine only 33 specimens of faeces from diseased pigs. Very little information could be discovered relating to the diseases with which the pigs were affected. No salmonellae were isolated from these samples.

Sheep

Healthy Sheep.—Specimens of faeces were examined from 500 healthy sheep. These were obtained in batches of approximately 20 specimens a week from a small abattoir receiving animals from many parts of the country. No salmonellae were isolated from these samples.

Diseased Sheep.—Specimens of faeces from 130 diseased sheep were received through the help of several veterinary diagnostic laboratories. These animals were suffering from a variety of diseases, the most common being parasitic gastro-enteritis. No salmonellae were isolated from these samples.

Goats

Diseased Goats.—It was found impossible to collect a sufficient number of faecal samples from healthy goats. Specimens, however, were examined from 100 diseased goats. These specimens were obtained from a laboratory which was responsible for the examination of faeces for intestinal parasites. Very little information was obtained about the diseases affecting these goats, but some of them were suffering from parasitic gastro-enteritis. None of the 100 specimens were shown to contain salmonellae.

Chickens

Healthy Chickens.—The total number of specimens examined from normal apparently healthy adult chickens was 750. Of these, 360 were obtained from Poultry Stock Improvement Plan (P.S.I.P.) flocks—that is, flocks in which *Salm. pullorum* infection is controlled by regular agglutination tests. These specimens were carefully selected so that normally not more than one chicken was sampled from any one farm unless the number of poultry on the farm was very large. Most of the specimens were collected by the veterinary staff of the Ministry of Agriculture and by members of the National Agricultural Advisory Service. The remaining 390 specimens were obtained from chickens in non-designated flocks. Some of these were collected by the method employed in the case of the P.S.I.P. chickens. The majority, however, were obtained from sales yards —a method of collection which was rapid and also ensured a wide distribution, as only one chicken was sampled from any one flock. Salmonellae was isolated from five (0.67%) of the 750 faecal specimens. All the positive specimens came from chickens belonging to non-accredited flocks. The organisms were *Salm. typhi-murium* (2), *Salm. pullorum* (2), and *Salm. anatum.* The five cultures were obtained after selenite enrichment. Tetrathionate cultivation resulted in the isolation of only one strain of *Salm. typhi-murium* and one of *Salm. pullorum.* Only one of the cultures, *Salm. pullorum,* was also isolated by direct plating on D.C.S.S. medium.

Diseased Chickens.—Faecal specimens from 500 adult chickens that were known to have died from causes other than primary salmonella infection were received

from a number of veterinary diagnostic laboratories in Britain. It was not possible to classify the chickens according to whether or not they were from P.S.I.P. flocks. Not more than one chicken from any one flock was examined. The causes of death of the chickens were various, and were considered to be typical of the losses occurring in flocks in this country. Eight (1.6%) of the 500 faecal specimens from diseased chickens were found to contain salmonellae. The organisms were *Salm. typhi-murium* (4), *Salm. pullorum* (2), *Salm. thompson*, and *Salm. senftenberg*. All the cultures except one strain of *Salm. typhi-murium* were isolated after selenite enrichment, and all except two, *Salm. pullorum* and *Salm. senftenberg*, after tetrathionate enrichment. Only one of the cultures, *Salm. thompson*, was also obtainable by direct plating of the eight positive specimens on D.C.S.S. medium.

Show Poultry.—No salmonellae were isolated from specimens collected from 420 chickens exhibited at the National Poultry Show and the Dairy Show in London in 1949.

Ducks

Healthy Ducks.—The total number of faecal specimens examined from healthy adult ducks was 500. The majority were obtained through the co-operation of members of the British Water-fowl Association. Owing to the relatively small number of duck farmers in this country it was not possible to confine examination of faeces to only one duck on any one farm. When, however, more than one specimen was examined from one farm, care was taken to ensure that they originated from ducks kept in different units. The only exception to this rule was when the units comprised large numbers of ducks; more than one specimen was then taken. Salmonellae were isolated from faecal specimens from six (1.2%) of the 500 healthy ducks. The organisms were identified as *Salm. typhi-murium* (5) and *Salm. meleagridis*. Three of the cultures were isolated after both selenite and tetrathionate enrichment; two were isolated after selenite enrichment only and one after tetrathionate only. Only one salmonella culture was isolated by direct plating on D.C.S.S. medium.

Show Ducks.—Salmonellae were not isolated from faecal specimens taken from 155 ducks exhibited at the National Poultry Show and the Dairy Show in London in 1949.

Turkeys

Healthy Turkeys.—With the help of members of the National Agricultural Advisory Service and individual turkey farmers it was possible to examine faeces from 650 adult turkeys. It was found necessary to examine more than one specimen from each turkey farm, but no more than one specimen was taken from each unit or pen. The only exception to this rule was made when large units containing several hundred turkeys were encountered. Salmonellae were isolated from the faeces of 16 (2.5%) of the 650 healthy turkeys. The organisms were *Salm. typhi-murium* (11), *Salm. anatum* (4), and *Salm. tennessee*. Ten of the cultures were obtained by both methods of enrichment, five after selenite enrichment only, and one after tetrathionate enrichment only. Direct plating on D.C.S.S. medium of the 16 positive faecal specimens resulted in the isolation of only two of the salmonella cultures.

Show Turkeys.—No salmonellae were isolated from the faeces of 63 turkeys exhibited at the National Poultry Show and the Dairy Show held in London in 1949.

Geese

Healthy Geese.—Owing to the methods of husbandry, technical difficulties made it impossible to collect a large number of faecal specimens from geese. Of the 100 specimens that were examined, all except 15 were taken from geese from different farms. These were mostly collected at poultry markets.

Salmonellae were isolated from the faeces of two (2%) of the 100 healthy adult geese. The organisms were identified as *Salm. thompson* and *Salm. typhi-murium*. The *Salm. thompson* culture was isolated by means of selenite and tetrathionate enrichment but not by direct plating. The *Salm. typhi-murium* culture was isolated after tetrathionate but not after selenite enrichment. This latter strain was also isolated by direct plating on D.C.S.S. medium.

Analysis of Results

Comparative Frequency of Salmonellae in Faeces of Different Species of Healthy Domestic Animals.—Table I is designed to compare the frequency with which salmonellae were isolated from faecal specimens of the different species of adult domestic animals that were examined. This table shows that turkeys were the most frequent faecal excreters of salmonellae, followed by geese, ducks, pigs, chickens, cows, and horses. As no salmonellae were isolated from the faeces of sheep it has to be concluded that they must be infrequent carriers. It is noteworthy that three species of poultry were the most frequent carriers of salmonellae. Variation between the different species appeared to be quite considerable; judging from the figures, turkeys were approximately four times more frequent excreters of salmonellae than chickens, six times more frequent than cows, and twelve times more frequent than horses.

TABLE I.—*Frequency with which Salmonellae were Isolated from Faeces of Adult Healthy Domestic Animals*

Species of Animal	No. Examined	No. Positive for Salmonellae	% Positive
Turkeys	650	16	2·5
Geese	100	2	2·0
Ducks	500	6	1·2
Pigs	600	4	0·67
Chickens	750	5 (3)*	0·67 (0·4)*
Cattle	750	3	0·4
Horses	500	1	0·2
Sheep	500	0	0

* The figures in brackets are the results of the isolation of salmonellae other than *Salm. pullorum*.

TABLE II.—*Frequency with which Salmonellae were Isolated from Faeces of Adult Animals Suffering from Diseases Other than Primary Salmonella Infection*

Species of Animal	No. Examined	No. Positive	% Positive
Chickens	500	8 (6)*	1·6 (1·2)*
Cattle	500	3	0·6
Horses	500	2	0·4
Sheep	130	0	0
Goats	100	0	0
Pigs	33	0	0

* The figures in brackets are the results of the isolation of salmonellae other than *Salm. pullorum*.

Comparative Frequency of Salmonellae in Faeces of Different Species of Diseased Animals.—Table II compares the frequency with which salmonellae were isolated from adult animals that were suffering, or had died, from diseases other than primary salmonella

infection. Chickens, cattle, horses, and sheep occur in the same order of frequency as was found in healthy animals of these species (Table I). The cattle and chickens were suffering from a variety of diseases; the eight salmonella-positive chickens and the three positive cows were all suffering from different diseases. Although the figures are higher than those for healthy animals, they do not lend much support to the view that salmonellae commonly proliferate in animals suffering from diseases caused by other agents.

TABLE III.—*Showing the Occurrence of Salmonella Types Isolated from Healthy and Diseased Animals*

Types of Salmonella	Total No. Isolated	% of Whole (50)	Species of Animal
Salm. typhi-murium	24	48	Turkey (11), chicken (6), duck (5), pig (1), goose (1)
Salm. dublin ..	7	14	Cow (6), horse (1)
Salm. anatum ..	5	10	Turkey (4), chicken (1)
Salm. thompson ..	4	8	Horse (2), chicken (1), goose (1)
Salm. pullorum ..	4	8	Chicken (4)
Salm. meleagridis ..	4	8	Pig (3), duck (1)
Salm. tennessee ..	1	2	Turkey (1)
Salm. senftenberg ..	1	2	Chicken (1)

Frequency of Isolation of Different Salmonella Types.—Table III illustrates the frequency with which different types of salmonellae were isolated during this work. Nearly half the number of salmonella cultures that were obtained were *Salm. typhi-murium*. This was by far the most common type isolated from turkeys, ducks, and chickens. The next most common types were *Salm. dublin, Salm. anatum, Salm. thompson, Salm. pullorum,* and *Salm. meleagridis.* As expected from data of clinical salmonella infection, *Salm. dublin* was most commonly found in cows, and was, in fact, the only type present in the faecal specimens from these animals. On the other hand, despite the fact that *Salm. pullorum* is by far the most common type causing clinical salmonella infection in chickens, it was not the type most commonly found in the faeces of the adult chicken in this country. It was also surprising that *Salm. thompson,* a common cause of disease in young chickens, was isolated only once from chickens but twice from horses.

Health and Infectivity of Faecal Excreters of Salmonellae

It was possible to examine more critically some of the animals that had been classified as healthy and that had been shown to be excreting salmonellae in their faeces. There was no evidence to indicate that the general health and condition of these animals were not normal.

In some cases it was possible to obtain faecal specimens from other animals on a farm where a faecal carrier of salmonellae had been found, and also to examine these animals on more than one occasion. Specimens from two horses kept in the same stable as a third horse which was a faecal excreter of *Salm. thompson* also contained this organism. Another horse, on different premises, remained a faecal excreter of salmonellae for six months, when examination was discontinued. Investigations following upon the isolation of *Salm. typhi-murium* from the faeces of a turkey showed that 26 of 30 turkeys in the same pen were also excreting this organism. Further examination about a month later revealed that most of the faecal specimens from these turkeys were still positive. A similar type of investigation in the case of another pen of turkeys revealed that 20 of 24 of these turkeys were also excreting *Salm. typhi-murium* in their faeces. The general health of both of these lots of turkeys was considered excellent. Their sera did not contain demonstrable antibodies to *Salm. typhi-murium.*

In contradistinction to this fairly permanent carrier state, examples of a temporary carrier state were also found. The faeces of a pig, examined several times after the isolation of *Salm. typhi-murium,* were consistently negative. Again, following upon the isolation of *Salm. typhi-murium* from the faeces of a duck, faecal specimens from all the ducks in the pen were examined, including, of course, the original duck. *Salm. typhi-murium* was not recovered from any of the faecal samples; two of the ducks were, however, excreting *Salm. give.*

Comment on Bacteriological Findings

Comparison of D.C.A. and D.C.S.S. Media for Faecal Examinations

For the first 150 specimens of bovine faeces Leifson's desoxycholate-citrate agar (D.C.A.) was used, and non-fermenting colonies from 84 specimens required further examination after selenite enrichment and 52 after tetrathionate enrichment. For the next 150 bovine specimens, D.C.A. with the addition of 1% sucrose and 1% salicin (D.C.S.S.) was used, and only 39 specimens required further examination after selenite and 38 after tetrathionate enrichment. The reason for the less noticeable effect of the addition of sucrose and salicin on the number of colonies requiring further examination after tetrathionate than after selenite enrichment was that their addition led to the recognition and elimination mainly of paracolon bacilli which grew more readily in selenite than in tetrathionate medium. *Proteus* strains, growing more commonly in tetrathionate than in selenite, did not ferment these substrates.

Comparison of D.C.S.S. With and Without Selenite and Tetrathionate Enrichment in Isolation of Salmonellae

This survey presented a good opportunity of comparing the value of plating on D.C.S.S. medium directly, and after enrichment in selenite medium and in tetrathionate broth. Tetrathionate broth is probably used more often than selenite medium as a routine procedure in the examination of faeces. Some workers report, however, that selenite is more satisfactory than tetrathionate (Hobbs and Allison, 1945; Cruickshank and Williams Smith, 1949; Preuss, 1949).

Table IV illustrates the comparative frequency with which salmonellae were isolated from the faecal specimens

TABLE IV.—*Showing the Comparative Value of Plating Faeces Direct on to D.C.S.S. Medium, and After Preliminary Enrichment in Tetrathionate and Selenite Media in the Isolation of Salmonellae*

Species	Total No. of Positive Specimens	Positive Selenite, Positive Tetrathionate	Positive Selenite, Negative Tetrathionate	Negative Selenite, Positive Tetrathionate	Positive for D.C.S.S.† (Direct)
Cattle ..	7	6	1	0	3
Horses ..	5	5	0	0	1
Pigs ..	4	2	2	0	0
Chickens	19	12	6	1	3
Turkeys ..	16	8	6	2	2
Ducks ..	6	3	2	1	1
Geese ..	3	2	0	1	2
Total ..	60*	38 (63%)	17 (28%)	5 (8%)	12 (20%)

* Several positive specimens from "in-contact" animals are included in this total.

† Results obtained by plating all positive samples direct on to D.C.S.S. medium.

by means of the different media. A few positive specimens from "in-contact" animals are also included. Of the 60 specimens shown to contain salmonellae, 38 (63%) were identified by both selenite enrichment and tetrathionate enrichment, 17 (28%) by selenite enrichment only, and 5 (8%) by tetrathionate enrichment only. Only 12 (20%) of the 60 specimens were shown to contain salmonellae by direct plating on D.C.S.S. medium. The superiority of selenite over tetrathionate medium was particularly noticeable in the case of the faecal specimens from turkeys, chickens, and pigs. Many of the plates originating from selenite-positive, tetrathionate-negative specimens grew only a small number of salmonellae colonies after selenite enrichment; tetrathionate enrichment of some of these specimens resulted in a prolific culture of *Proteus* colonies.

Types of Non-fermenting Colonies Growing on D.C.S.S. Medium Sown with Faeces of Different Animal Species

The bacterial flora of the different animal species differed from one another. Table V illustrates a few of these differences; the figures are percentages and relate to healthy animals. A great variation was noted in the *Proteus* content of the faeces of different animal species. The order of frequency of isolation of *Proteus* sp. from the various species was pigs, ducks, turkeys, sheep, chickens, cows, and horses, the actual percentage being 72, 56, 40, 38, 24, 16, and 12. *Proteus* strains were more commonly found after tetrathionate than after selenite enrichment. The number of faecal specimens containing paracolon bacilli that failed to ferment the sucrose or salicin in the D.C.S.S. medium did not show a great variation between the different species of animals, there being about 20% in all cases except sheep and pigs; the percentages for these two species were 60 and 40 respectively. No significant difference was noted between the numbers of paracolon bacilli and *Proteus* sp. present in the faeces of normal animals and diseased animals.

TABLE V.—*Showing the Frequency with Which Non-fermenting Colonies were Isolated on D.C.S.S. Medium from the Faeces of Different Healthy Animals*

Animals	Bacterium	% Positive on D.C.S.S.		Total % of Positive Specimens
		Through Selenite	Through Tetrathionate	
Cattle ..	*Proteus*	10	12	16
	Paracolon bacilli	16	11	22
Horses ..	*Proteus*	6	9	12
	Paracolon bacilli	16	14	22
Chickens ..	*Proteus*	12	20	24
	Paracolon bacilli	17	6	20
Turkeys ..	*Proteus*	19	31	40
	Paracolon bacilli	17	12	24
Ducks ..	*Proteus*	25	54	56
	Paracolon bacilli	25	11	28
Pigs ..	*Proteus*	32	70	72
	Paracolon bacilli	30	20	40
Sheep ..	*Proteus*	20	32	38
	Paracolon bacilli	43	45	60

A Comparison of Screening Methods

Two methods of screening the non-fermenting colonies growing on D.C.S.S. plates were compared. Usually the screening was carried out by rapid testing of suspicious colonies for urease and indole production. Sometimes, however, colonies were submitted to a rapid slide-agglutination test using the polyvalent O serum issued by the Standards Laboratory. First impressions were that this latter test was less time-consuming, but in view of the considerable number of colonies that either partly or completely agglutinated the polyvalent O serum, or were either auto-agglutinable or sticky, the former test was preferred. When using polyvalent O serum for screening it was found necessary to test agglutinating strains for urease and indole production at an early stage to avoid a lot of unprofitable and time-consuming work.

After the preliminary tests, cultures were purified. The D.C.A. plates modified by replacing lactose with dulcitol were extremely useful for this purpose. It was found possible to plate out six cultures on each plate so as to obtain isolated colonies. The salmonella cultures on this medium produced either pink colonies or paler colonies with black centres. Very few indeed of the cultures that were investigated, and which were not salmonellae, produced this reaction. An exception had to be made for *Salm. pullorum*, which does not ferment dulcitol. It must be emphasized that this medium was used mainly to obtain pure cultures, and cultures were not discarded if they did not give a positive reaction.

Discussion

The results of this survey show that the types of salmonellae isolated from the faeces of healthy animals were, with the possible exception of *Salm. pullorum*, those that are commonly incriminated in outbreaks of food-poisoning (M.R.C. Report, 1947). They are also the types that commonly cause clinical disease in domestic animals. It is therefore obvious that symptomless faecal excreters of salmonellae are important from both the public health and the agricultural points of view.

Most of the outbreaks of food-poisoning traced to domestic animals have originated from "emergency-slaughtered" or "casualty" animals. This does not mean that these animals are the most common source of infection, as the vast majority of outbreaks remain untraced (Food Poisoning in England and Wales, 1941–8). The attention of those concerned with the investigation of outbreaks of food-poisoning is naturally directed upon these animals, whereas outbreaks caused by animals that are symptomless faecal carriers would tend to go untraced. Extensive outbreaks, probably caused by symptomless faecal excreters, have, however, been reported (Camps, 1947; Jones and Symons, 1948). That salmonella infection in man is closely related to infection in animals has been shown by Watt and DeCapito (1950) in America. Whenever they discovered a human salmonella excreter they examined faecal specimens from the domestic animals within one block radius. In 50% of cases they were able to isolate from one or more of the animals the same type of salmonella as from the human excreter. Hinshaw, McNeil, and Taylor (1944) also have drawn attention to cases of gastro-enteritis among attendants on poultry farms which have occurred simultaneously with outbreaks of clinical salmonella infection among the poultry. They are of the opinion that in some instances agricultural workers may be the sources of infection for poultry.

The relative importance of different species of animals as reservoirs of salmonella infection depends on the incidence of salmonella carriers in the species, the total population of the species, and, in the case of food-poisoning, the degree of contact they have with human beings and their food. The figures for the total population of some of the species, based on the June,

1950, Livestock Census, are: horses, 500,000; cattle, 8,000,000; pigs, 2,200,000; chickens, 60,000,000; ducks, 2,200,000; turkeys, 750,000; and geese, 800,000. The correlation of these figures with those in Table I shows that merely comparing the frequency of salmonella excreters among different species of animals does not necessarily give a true impression of the importance of the different species as reservoirs of salmonellae. For instance, although the frequency of salmonella excreters among chickens was low, their large population makes them probably the largest reservoirs of infection. Turkeys, found to be the most frequent faecal excreters of salmonellae, do not appear to be so important as a reservoir. They may, however, be of considerable significance as foci of infection and may disseminate it to other species of animals with which they may come in contact. Horses are probably of little importance.

From the food-poisoning point of view, cattle, sheep, and pigs are important, as they are the principal food animals. Symptomless faecal excreters of these species may give rise to infection of human beings after the contamination of meat at slaughter by the accidental rupture of the alimentary tract, or by the contamination of slaughtering instruments, and of the slaughterhouse itself, with faeces containing salmonellae; cloths used for wiping down the carcass may be particularly dangerous in this respect. The excretion of salmonellae in the faeces of milking-cows is an added danger in view of the possibility of the milk becoming infected; many of the outbreaks of food-poisoning caused by *Salm. dublin*, the most common type isolated from cattle, have been traced to contaminated milk. The importance of raw or insufficiently cooked eggs as sources of infection in man has already been indicated, particularly in the case of duck eggs. The contamination of poultry during evisceration may also be of importance, particularly as this process is often carried out by those responsible for the preparation of food.

The difficulties in preventing animal faecal excreters giving rise to salmonella infection in human beings and in other animals are formidable. The detection of carriers by agglutination tests is effective in the control of *Salm. pullorum* infection in chickens, but such methods are much less effective in other salmonella infections. There is no evidence to suggest that vaccination or chemotherapeutic substances would reduce the number of carriers of salmonellae. It may be possible that improvements in general hygiene and management would result in a decrease in the frequency of salmonella carriers. Some support for this is given by the finding that no salmonellae were isolated from the faeces of animals exhibited at the Dairy Show and the Poultry Show in London in 1949, as these animals would have been kept under a better standard of hygiene than ordinary commercial animals. However, another explanation of this fact may be that the general condition of a faecal excreter of salmonellae would not be of the very high standard required for exhibition at these shows. From the food-poisoning point of view it is obvious that more attention will have to be paid to hygiene during and after the slaughter of food animals if the dangers of animal excreters of salmonellae are to be reduced.

Summary

In a survey of healthy adult domestic animals in England and Wales, 16 of 650 turkeys (2.5%), two of 100 geese (2%), six of 500 ducks (1.2%), four of 600 pigs (0.67%), five of 750 chickens (0.67%), three of 750 cows (0.4%), one of 500 horses (0.2%), and none of 500 sheep were found to be excreting salmonellae in their faeces. The organisms from the turkeys were *Salm. typhi-murium* (11), *Salm. anatum* (4), and *Salm. tennessee*; from the geese, *Salm. typhi-murium* and *Salm. thompson*; from the ducks, *Salm. typhi-murium* (5) and *Salm. meleagridis*; from the pigs, *Salm. meleagridis* (3) and *Salm. typhi-murium*; from the chickens, *Salm. typhi-murium* (2), *Salm. pullorum* (2), and *Salm. anatum*; from the cows, *Salm. dublin* (3); from the horse, *Salm. thompson*.

Among animals suffering from diseases other than primary salmonella infection, eight of 500 chickens (1.6%), three of 500 cows (0.6%), two of 500 horses (0.4%), and none of 130 sheep, 100 goats, and 33 pigs were found to be excreting salmonellae in their faeces. Although these figures are higher than those for healthy animals they do not lend much support to the view that salmonellae commonly proliferate in disease processes. The organisms from the diseased chickens were *Salm. typhi-murium* (4), *Salm. pullorum* (2), *Salm. thompson*, and *Salm. senftenberg*; from the diseased cows, *Salm. dublin* (3); and from the diseased horses, *Salm. dublin* and *Salm. thompson*.

No salmonellae were isolated from the faeces of the following species of animals which were exhibited at national shows in this country: cows (430), chickens (420), ducks (155), and turkeys (63).

All the salmonella types that were isolated in this survey, with the possible exception of *Salm. pullorum*, are known to be capable of causing disease in man.

The significance of these findings is discussed with regard to the causation and prevention of food-poisoning in man and the control of disease in animals.

The techniques used in the isolation and identification of the salmonellae are also discussed. Selenite medium was found to be superior to tetrathionate broth as an enrichment medium, but a greater number of positive specimens were found by the use of both media.

We are greatly indebted to Mr. K. A. Piggins, Miss Sheila Day, and Mr. J. F. Tucker for the efficient and untiring manner in which they have helped us with the technical aspects of this work. We also wish to thank Dr. Joan Taylor for typing some of the salmonella cultures. Our thanks are also due to Professor Wm. C. Miller and Dr. R. F. Gordon for help in organizing this survey, and to the numerous people who, by collecting faecal specimens, gave us aid without which this survey would have been impossible to carry out.

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A note in *Nature*, May 5, page 730, draws attention to the unreliability of killing the eggs of worms in faeces with formalin. A faecal specimen from a patient infected with *Ascaris lumbricoides* was preserved in hot 10% formalin in March, and when the specimen was examined in November many eggs were found containing motile Ascaris larvae, although the formalin concentration was still 6%.

A STUDY OF HEPATIC FUNCTION IN MAN BEFORE AND AFTER PARTIAL RESECTION OF LIVER

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It is well known that "liver-function tests" may be negative in the presence of extensive liver disease and that sometimes one of these tests may be positive whilst others are negative. Recently the opportunity arose of investigating liver function in a patient before and after partial resection of the liver, and the findings are recorded as an indication of the effects of simple reduction of liver tissue on these tests. In a survey of the literature recording partial hepatectomy in man we have been unable to find biochemical studies similar to those here recorded, and Berman (1951) does not mention such an investigation. However, Grey Turner (1923) recorded faecal fat, urinary ammonia, and urinary urea findings two years after resection of a hepatoma in a boy aged 13.

Case Report*

A man aged 54 was admitted to hospital with acute abdominal pain, and at a laparotomy performed by Mr. A. G. Riddell two nodules were found in the left lobe of the liver, from one of which haemorrhage was occurring. The bleeding nodule was excised and haemostasis was secured. Histological examination of the biopsy specimen showed it to be a primary liver-cell carcinoma, bile pigment being present in the neoplastic cells; there was no evidence of cirrhosis in the surrounding liver tissue.

*A separate communication describing the surgical procedure followed and the pathological features of the tumour is being prepared by Mr. A. G. Riddell.

It was at this stage that the initial pathological investigations were carried out.

At a second operation for radical excision of the growth, also performed by Mr. Riddell, under thiopentone, curare, and nitrous oxide anaesthesia, the left lobe of the liver was removed by diathermy incision after ligation of the main vessels to the lobe. The excised portion of liver had a fresh weight of 215 g., and, like the organ as a whole, it showed no evidence of cirrhosis either macroscopically or microscopically. The remaining neoplastic nodule had a diameter of 1 cm.

During the immediate post-operative period, which was free from complications, the liver-function tests were all repeated.

The patient has remained well and gained weight during the nine months since his operation. There has been some increase in the size of the right lobe of the liver, presumably as a result of compensatory hyperplasia.

Method of Study

The following tests were performed before and after resection of the left lobe of the liver: (1) Tests related to protein metabolism: serum proteins, serum flocculation tests (colloidal red, cephalin cholesterol, thymol turbidity, and flocculation), plasma prothrombin concentration, plasma and urinary amino-acid patterns, blood urea. (2) Tests related to bile-pigment metabolism: serum bilirubin, urinary urobilin(ogen). (3) Tests related to detoxicating function: hippuric acid synthesis (intravenous test). (4) Tests related to excretory function: bromsulphthalein clearance, serum alkaline phosphatase.

These tests were carried out by standard techniques in common usage. The methods employed in the case of the amino-acid studies, however, require mention. The concentration of individual amino-acids was followed by the method of paper partition chromatography, two-way chromatograms being run as described by Dent (1947). In testing urines for a pathological output of amino-acids a urine volume with a constant amount of total nitrogen—that is, 250 μg.—was used (Dent, 1949). In the case of plasma a constant volume of 625 μl. of ultrafiltered and desalted fluid was taken. Each specimen of urine and plasma was examined—oxidized and unoxidized.

The results are summarized in Table I.

TABLE I.—*Results of Tests*

Test	Pre-resection Results		Post-resection Results			
	Days Pre-op.	Pre-operative Results	Days Post-op.	Immediate Post-operative Results	Days Post-op.	Late Post-operative Results
Serum proteins	14	Total 5·4 g.%: albumin 3·5 g., globulin 1·9 g. A/G 1·8	5	Total 5·5 g.%: albumin 3·9 g., globulin 1·6 g A/G 2·4	54	Total, 7·7 g %: albumin 4·4 g., globulin 3·3 g. A/G 1·3
					108	Total, 8·0 g.%: albumin 5·1 g., globulin 2·9 g. A/G 1·8
Colloidal red	14	Negative (0)	5	Positive (++)	54	Weak positive (+)
					108	Weak positive (+)
Cephalin cholesterol	14	Negative (0)	5	Very weak positive (±)	54	Negative (0)
					108	Negative (0)
Thymol turbidity and flocculation	14	5 units with flocculation	5	10 units with flocculation	54	8 units with flocculation
					108	7 units with flocculation
Plasma prothrombin concentration	14	91% of normal	5	91% of normal		
Plasma amino-acid pattern	7	Normal	3	Abnormal but typical of post-operative state		
Urine amino-acid pattern	14 and 7	Slight abnormality—probably legacy of first operation	1–7	" " "		
Blood urea	7	39 mg./100 ml.	5	39 mg./100 ml.		
Serum bilirubin	5	Direct, negative; indirect, 0·4 mg./100 ml	5	Direct, negative; indirect, 0·4 mg./100 ml.		
Urine urobilin(ogen)	7	Normal	1–7	Excess on days 2–7. Peak excretion on 6th day		
Hippuric acid synthesis* (intravenous test)	6	Excretion in 1 hour, 0·64 g.	12	Excretion in 1 hour, 0·76 g.		
Bromsulphthalein clearance (dose 5 mg./kg.)	10	Retention at 1 hour, less than 2%	7	Retention at 1 hour, less than 2%		
Serum alkaline phosphatase	5	6 King-Armstrong units/100 ml.	5	4·5 King-Armstrong units/100 ml.		
Urea clearance	1	C_s = 81% and 70% of average normal				

* Normal excretion corrected for body weight (Scurry and Field, 1943) = 0·70–1·25 g.

Discussion

It is important in considering the results to estimate the proportion of liver tissue that was removed. Using the formula of Scurry and Field (1943)—namely, liver weight = 0.433 oz./lb. body weight—the theoretical liver weight calculated on the patient's maximum known weight is, in this case, 1,380 g.; hence about 16% of the organ was removed.

Before the results of some of the tests are discussed certain points applicable to the interpretation of all must be mentioned. First, there is the enormous functional reserve of the liver. Secondly, there is the remarkable speed of regeneration. In the rat, after removal of over 60% of the organ regeneration is complete in 10 to 21 days (Warner, 1938; Abercrombie and Harkness, 1951). Whilst it is probable that the rate of regeneration will be slower in a man of 54 years this factor may have played a part in the normal post-resection results. Finally, it must be remembered that in this case the primary carcinoma developed in a non-cirrhotic liver. In adults this is a circumstance of great rarity (Counseller and McIndoe, 1926; Tull, 1932; Boyd, 1944; Hoyne and Kernohan, 1947; Willis, 1948; Mallory, 1948; Berman, 1951).

The further discussion is here confined to those tests which showed a significant change after the resection.

Serum Proteins

The initial estimation showed a rather low total protein. This low reading may well have been a result of the haemorrhage, despite a transfusion of 4 pints (2.27 litres) of blood after admission. The very much higher results found at follow-up are probably to be attributed to the replacement of the serum proteins lost at the time of the haemorrhage.

Serum Flocculation Tests

The thymol test alone registered an abnormality before the resection; moreover, the occurrence of flocculation in this reaction is stated to indicate abnormal liver function (Maclagan and Bunn, 1947; Neefe *et al.*, 1950). Possibly this result is to be attributed to the presence of the carcinoma.

It can be seen (Table I) that in the immediate post-operative phase the colloidal-red and cephalin-cholesterol flocculation tests changed from negative to positive and that the thymol turbidity registered a greater degree of abnormality. Whilst the cephalin-cholesterol test had returned to normal in two months the colloidal red and thymol turbidity were still abnormal three months after operation.

In order to ascertain that the changes in the flocculation reactions were related to the liver resection, control tests were performed. These control observations were carried out on two cases of carcinoma of the pancreas, both found at laparotomy to have hepatic metastases, and on a case of carcinoma of the oesophagus subjected to radical surgery. A further control observation was made on a case in which a pedunculated secondary carcinoma of the liver, weighing 125 g., was excised. In all four the flocculation tests were negative one week after operation.

There is the possibility that the initial results may have been altered by dilution of the gamma globulin following transfusion. However, in the case of the post-resection results the dilution factor must again be taken into consideration, as the patient received a further 2 pints (1.14 litres) of blood during the operation. A change in these tests means in effect that there has been a qualitative change in the serum proteins—in the globulin or the albumin fraction, or in both. In clinical terms, such a change is less likely to be due to a reduction in liver mass than to a necrosis of liver cells. There would be ample opportunity for such to occur locally, both from the use of the diathermy knife and the ligation of the vessels to the left lobe, with the consequent disorganization of the intrahepatic circulation. However, the amino-acid studies gave no indication of necrosis. Thus it is of interest that Popper *et al.* (1949) believe that the thymol test remains positive during regeneration and distorted reconstruction of the liver.

Plasma and Urinary Amino-acid Patterns

It has been reported (Dent and Walshe, 1951) that certain changes are commonly found in the urinary excretion of amino-acids after abdominal surgery, particularly if the liver or biliary tract is involved. The initial chromatograms, following the first operation, showed minor abnormalities that do, in fact, fall within this category. After resection of the left lobe of the liver much greater alterations in amino-acid excretion were expected, because of the major disturbance in hepatic circulation and the necrosis that must have been produced. This was not the case, and only the usual post-operative response was observed. Figs. 1 and 2 show the patterns detected in the urine and plasma on the third post-operative day. The changes in the plasma were no more striking than those in the urine, the only abnormality being a definite rise in the cystine concentration. These findings accord well with those of Ferrari and Harkness (1951), who made similar studies on the rat after removal of two-thirds of the liver. In view of the dramatic rise of liver ethanolamine phosphoric acid reported by these workers as occurring 24 hours after operation, it is of some interest that our patient was excreting this compound, as the principal ninhydrin reactor in his urine, six months after operation. One further abnormality appears to merit attention

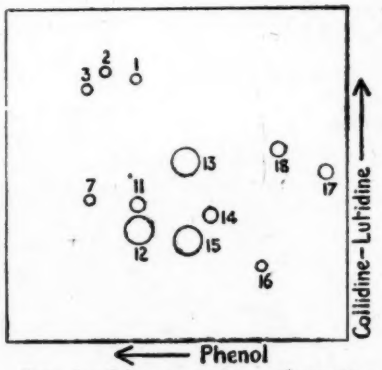

FIG. 1.—Diagram of a chromatogram from urine with a nitrogen content of 250 μg. oxidized. Specimen collected on the third post-operative day.

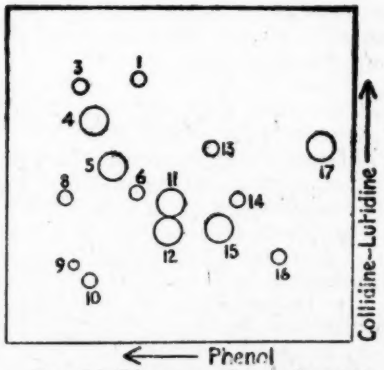

FIG. 2.—Diagram of a chromatogram from 625 μl. of plasma ultrafiltrate oxidized. The plasma was collected on the third post-operative day.

KEY.—1 = Tyrosine. 2 = Tryptophan. 3 = Phenylalanine. 4 = Leucine. 5 = Valine. 6 = α-Amino-butyric acid. 7 = "T" spot.* 8 = Proline. 9 = Arginine. 10 = Lysine. 11 = Alanine. 12 = Glutamine. 13 = Taurine. 14 = Serine. 15 = Glycine. 16 = Glutamic acid. 17 = Cysteic acid (from cystine). 18 = Unknown.

*"T" spot has since been identified as β-amino-isobutyric acid. (Crumpler, H. R., Dent, C. E., Harris, H., Westall, R. G., *Nature, Lond.*, 1951, **167**, 307).

—that is, the presence of a ninhydrin reactor (Fig. 1, symbol 18) not reported by Dent (1948) as occurring in human urine. Work on the isolation and identification of this compound will form the basis of a separate communication. In conclusion it can be said that resection of 16% of the liver produced no specific change in amino-acid metabolism.

Urinary Urobilin(ogen)

Before resection the excretion was within normal limits. During the eight days immediately following operation the excretion was excessive on five days, the peak being reached on the sixth day. This was in fact a quantitative change in the excretion of urobilin(ogen), as allowance was made for variations in the 24-hour urine volumes. Control observations were made on eight cases following surgery of comparable severity. The results are shown in Table II. Reference to this table shows that, while several of the controls did have excess urobilin(ogen) excretion post-operatively, in none was it manifest so early or so markedly as in the patient subject to partial hepatectomy. It seems possible, therefore, that part of this increase is directly attributable to decrease of liver mass available for disposal of the chromagen arriving via the portal vein.

TABLE II

Operation	Pre-op. Day	Post-op. Days							
	1	1	2	3	4	5	6	7	8
Part. hepatectomy	–	–	+	+	0	++	+++	++	–
Part. gastrectomy	–	0	–	–	–	–	–	–	
,, ,,	–	–	–	–	–	–	–	–	
Lobectomy ..	–	–	–	–	–	–	–	0	
Thoracoplasty ..	–	0	0	–	+	+	++	0	
Laminectomy ..	–	0	–	–	–	–	–	–	
Oesophagectomy	–	–	–	–	++	+++	++	0	
Cholecystectomy (without biliary drainage) ..	–	+	–	–	–	–	–	–	
Blood transfusion (3 pints) ..	–	–	–	–	–	–	–	–	

0, no specimen; –, no excess urobilin(ogen); +, slight excess; ++ moderate excess; +++, marked excess.

Further control observations on a patient who received a transfusion of 3 pints (1.7 litres) of blood established that this alone was not likely to be responsible for the increased urobilin(ogen) in the urine following the resection.

Summary and Conclusions

Liver-function tests were performed before and after resection of 16% of the liver in a case of primary liver-cell carcinoma occurring in a non-cirrhotic organ.

The serum flocculation tests and the urinary excretion of urobilin(ogen) alone showed changes believed to be attributable to partial resection of the liver.

The serum proteins and the pattern of amino-acids in the blood and urine showed changes which are believed to be non-specific in relation to the operation.

The following tests failed to register the surgical intervention: plasma prothrombin concentration, blood urea, serum bilirubin, hippuric acid synthesis, bromsulphthalein clearance, serum alkaline phosphatase.

We wish to thank Mr. H. R. I. Wolfe, the surgeon in charge, for permission to publish this report, and Mr. A. G. Riddell, through whose co-operation we were able to carry out this investigation.

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BONE DYSTROPHY IN ASSOCIATION WITH MUSCULAR DYSTROPHY (MYOPATHY)

BY

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In 1905 Professor Spiller stated that implication of the bones in progressive muscular dystrophy was not often observed, and that many of the textbooks on nervous diseases made no mention of it. This statement is almost as true now as it was then, and, although bone changes in poliomyelitis, syringomyelia, and other neuromuscular disorders are frequently described in standard textbooks, their association with primary muscular dystrophy is rarely mentioned.

Marie and Crouzon (1903) reported a case of muscular dystrophy with fracture and atrophy of the humerus. Spiller (1905), in an account of a case of muscular dystrophy with wasting of the humerus scapula, and acromion process, gave as his earliest reference that of Lloyd (1884); however, Friedreich had discussed the subject at length in 1873 and had referred to an earlier observation of Le Gendre.

Bone changes mentioned in the literature include not only kyphoscoliosis and deformities of the skull, foot, and pelvis, but also atrophy of the clavicles, scapulae, ribs, and innominate bones, and atrophy, narrowing, and, less frequently, shortening of the long bones. The latter have often a shaft of reduced width, the reduction of the medullary canal being more marked than that of the cortex, whereas the epiphyses may be of normal diameter, giving an attenuated dumbbell shape to the affected long bones. Zellweger (1946) described five patients whose pelves were *x*-rayed, and who were said to have coxa valga; one was shown to have bilateral dislocation of the hips with hypoplasia of the acetabula.

FIG. 1.—Profile of patient, showing typical stance with lordosis, feet astride, and scapulae winged.

The patella in one case, by loss of its bony structure, resembled a thin-walled cyst described by Merle and Raulot-Lapointe (1909) as "rotule de verre."

In discussing causes most authors discount muscular inactivity. Curschman (1936) often found no bone atrophy in advanced muscular dystrophy. Maybarduk and Levine (1941) pointed out that bones were affected which could hardly have been influenced by muscular disuse—for example, shortening of the vertical ramus of the lower jaw was noted, though masticatory muscles were not involved in the dystrophy. They referred to Eulenburg's (1896) case of muscular dystrophy, in which both atrophy and hypertrophy of the bones were found.

In describing the following case we again draw attention to the occurrence of bone changes in primary muscular dystrophy.

Case Report

A woman aged 28 was admitted to hospital on July 19, 1949. At the age of 12 she fell from a gate, fracturing her right clavicle. One year later she noticed a weakness of her arms, which she at first attributed to her fall. The weakness affected the muscles of the upper arms and shoulders, so that she could not get her hands up to do her hair and had to support her elbows on the dressing-table. She received massage treatment without improvement, but the condition did not seem to get any worse until the birth of a stillborn child in 1942 after a pregnancy complicated by high blood pressure. After the puerperium the left leg appeared to be weak and heavy, and her muscles ached after exertion. The condition of the arms did not seem to have deteriorated.

Examination showed the patient to be a well-nourished young woman, weight 8 st. 13 lb. (56.7 kg.), height 5 ft. 2 in. (157.5 cm.). There was marked lordosis (Fig. 1) with compensatory upper dorsal kyphosis, and bilateral talipes equinovarus. Both shoulder-blades appeared to be small, the left measuring 6 in. (15 cm.) along its vertebral border, the right 5½ in. (13.8 cm.). They were highly placed, giving a Sprengel's type of shoulder deformity, and were also winged. The gait was of "myopathic" type, and it had been originally suggested that she might have a congenital dislocation of the hip. On attempting to rise from the floor, she went through the evolutions known as "Gowers's pathognomonic figures."

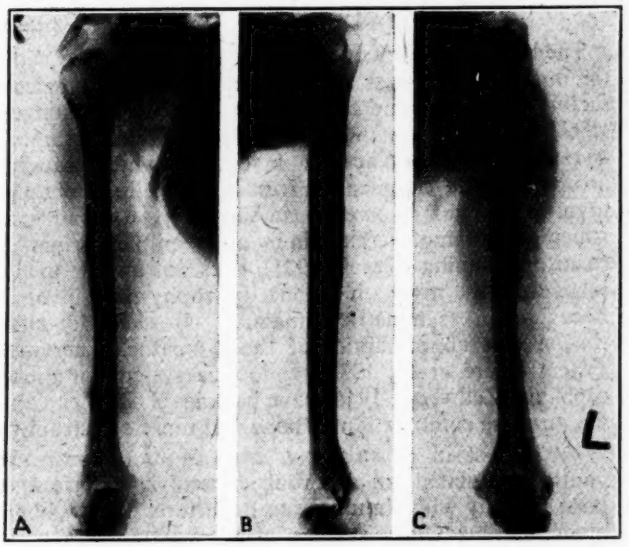

FIG. 3.—A. Patient's right humerus. B. Left humerus of a normal control of same age and height. C. Patient's left humerus. Note the attenuated dumbbell appearance given to the patient's right humerus by the comparatively slender shaft. The medullary diameter is much reduced though the cortex is of average depth.

There was weakness of the shoulder girdle muscles, particularly deltoids, pectoralis major, trapezius, rhomboids, and serratus magnus. The left trapezius and both deltoids were wasted, though facial musculature and sternomastoids appeared normal. The muscles of the arms and forearms were also involved, particularly the triceps and brachioradialis on the right side, with 1 in. (2.5 cm.) of wasting of the right arm. There was no loss in the power of grip. The arm reflexes were uniformly diminished, with the exception of the left supinator jerk. Weakness also involved the legs, so that flexion of the hip and knee, dorsiflexion, plantar flexion, and eversion of the feet were difficult. These changes were more marked in the left leg and thigh, and the left thigh showed ¾ in. (1.9 cm.) wasting. The abdominal muscles were all extremely weak, and so were the sacrospinalis group, particularly on the left side. There was no pseudo-hypertrophy of the affected muscles and they did not fibrillate. There were no sensory, pyramidal tract, or cerebellar abnormalities.

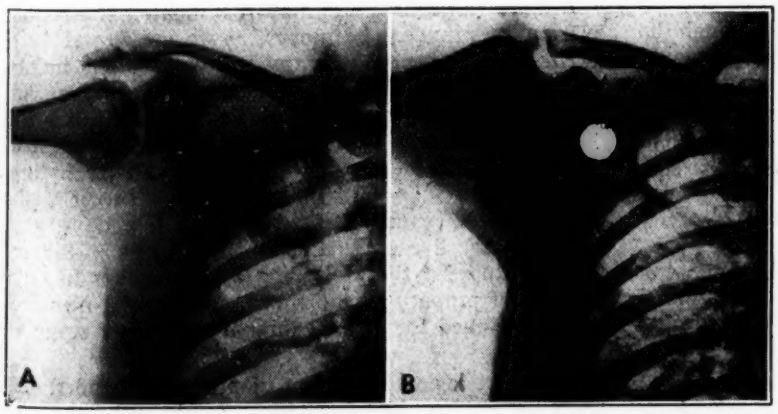

FIG. 2.—Showing the elevated hypoplastic right scapula of the patient (A) compared with that of a normal control (B). In taking these pictures care has been made to avoid foreshortening of the scapula by obliquity.

Radiographs of the arms and shoulder girdles showed the right scapula to be elevated and hypoplastic (Fig. 2). The left scapula, though by no means as underdeveloped as the right, was also on the small side. The right humerus was shorter than the left, and was also shorter than a well-selected control (Fig. 3). The right humeral shaft was narrow, the medullary diameter being much reduced, while the cortex was of average depth. The extremities of the humerus were nearly normal in size, and the cancellous texture was not altered. No overall reduction in calcium content was indicated by the *x*-ray films. Radiographs of the rest of the skeleton revealed no abnormality, there being no hip dislocation.

The patient's three sisters and one brother, and a nephew aged 2½, were examined clinically and radiologically, but showed no evidence of either myopathy or bone dystrophy.

Discussion

The bone dystrophy of myopathy has in common with the muscular weakness only one undisputed aetiological factor, which is a heredo-familial incidence (Schultze, 1899; Dreyer, 1906; and others). Spiller (1898) assumed a process taking place in myopathy which caused atrophy and developmental arrest in early life, probably involving bones as well. Hemiatrophy, a condition which one attempts to explain by an incomplete minimal form of twinning (Gesell, 1921), does not appear to be related, as the myopathic bone dystrophy may involve bones in an asymmetrical manner. It is hardly surprising that abnormalities of the sympathetic nervous system (Kuré *et al.*, 1936), endocrine system, or diencephalon (Zellweger, 1946) have been invoked to explain the puzzling combination of bone and muscle dystrophy.

Friedreich, in describing a case of an 18-year-old youth, postulated an external concentric progressive bone atrophy with simultaneous deposition of new bone along the medullary surface of the cortex. He considered the process to be a nutritional atrophy rather than an arrest in development.

Despite the numerous points of similarity between this humerus and one whose development has been arrested or slowed down by paralysis—for example, acute anterior poliomyelitis—it is not easy to explain all characteristics by disuse in the absence of any osteoporosis in this case. Even the versatility of Pommer's (1925) theories of tissue pressure as a basis for the mechanism of changes in blood supply causing relative preponderance of osteoclastic or osteoblastic activity does not provide a ready explanation of why the bone should be abnormally slender and of normal density in this case. If these bones have ever been of normal dimensions the present appearances must be due to the process postulated by Friedreich. Even if the bones have developed in this fashion (never having been normal) the compactum must partially, at least, have been laid down from within in order to explain the alterations in cortex/medullary ratio. Nevertheless, the final result in this condition, as in poliomyelitis, is in striking contrast to the thick sturdy bone with prominent muscle attachment produced by continued heavy muscular stresses. It would be impossible to assess whether developmental arrest had occurred from the time that muscular weakness became evident in this case; the question could be answered only by repeated observation of progressive cases beginning at an early stage.

Trophic changes are not operative in the same sense as they are in tabes when kinaesthetic sensation is commonly involved and Charcot's joints occur, although the word "trophic," meaning a nutritional change, would be applicable.

Apart from recognizing familial incidence in both muscle and bone changes, we feel that there is little to be gained by theorizing upon the pathogenesis of the bone changes.

Summary

A case of myopathy showing atrophy and hypoplasia of humerus and scapula is described. Previous literature is reviewed and possible mechanisms are briefly discussed.

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A CASE OF PRIMARY AMENORRHOEA ASSOCIATED WITH ASTHMA

BY

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The Physiology of Primary Amenorrhoea

The mechanism responsible for menstruation may be interrupted at three levels: first, the output of pituitary gonadotrophins may not suffice to stimulate the ovary to secrete oestradiol, to ovulate, and to secrete progesterone; secondly, the ovaries may be unable to respond to a normal pituitary gonadotrophic stimulus; and, thirdly, the uterus may not respond to the ovarian hormones. Primary amenorrhoea may arise at any of these levels. Pituitary deficiency may be of all degrees from the extreme of pituitary dwarfism, through decreasing grades of gonadotrophic hypoplasia, to a mere delay in the establishment of puberty and menstruation. Ovarian deficiency similarly ranges from complete agenesis to the mildest hypoplasias. An infantile uterus is only rarely seen when ovarian secretion is normal, but undue delay in the establishment of menstruation may leave the uterus irreversibly infantile.

There is little hope of curing primary amenorrhoea if an infantile body-build indicates severe pituitary hypoplasia, or if extreme ovarian deficiency is shown by a eunuchoid body-build (hormonal castrate). Success is most likely in the obese type of young woman who may perhaps be regarded as having no more than a very undue delay of puberty.

Primary amenorrhoea may be treated by either ovarian or pituitary hormones. At the lowest level intermittent oestrogen therapy will very often induce cyclical withdrawal haemorrhage from the uterus. Such bleeding may give psychological benefit, but is too far removed from the normal mechanism of menstruation to induce a normal pituitary–ovarian rhythm. Better results follow when progesterone succeeds the oestrogen—for example, oestrogen for five days, progesterone for five days, and 20 days' rest. Bickers (1948) induced cyclical bleeding by this means in 60% of cases of primary amenorrhoea, and in 40% menstruation continued for at least three months after stopping treatment.

The most logical treatment of primary amenorrhoea, however, is to stimulate or reinforce the normal pituitary secretion of follicle-stimulating and luteinizing hormones. Suitable cases often respond to massive

doses such as five daily injections of 3,000 i.u. of serum gonadotrophin followed by three injections of 1,500 i.u. of chorionic gonadotrophin on alternate days (Riisfeldt, 1949). The treatment may, however, be interrupted either because antihormones to the serum gonadotrophin form or because the patient becomes allergic to other components of the mare's serum. The proprietary preparation "synapoidin" avoids this difficulty by combining chorionic gonadotrophin with a "synergistic" pituitary extract; the preparation is said to exert both follicle-stimulating and luteinizing effects, and encouraging results in the treatment of amenorrhoea of pituitary origin were reported by Davis (1944).

Either form of pituitary therapy may sometimes excessively stimulate the ovaries. The patient suffers severe abdominal pain and the ovaries are greatly enlarged by cystic changes, with haemorrhages into cysts and interstitial tissue. The ovaries invariably return to normal within three weeks of stopping treatment (Movin, 1949).

Allergy and Menstruation

The association of ovarian and especially of menstrual disorders with allergic manifestations has often been noted. Thus, cases of skin hypersensitivity which vary with the stage of the premenstrual cycle are not infrequently observed, and premenstrual and menstrual migraine are also well-known entities. The association of asthma and menstruation is perhaps less well known, but certain well-defined groups occur. First, there are those children who have asthma till the age of puberty and who at the menarche are completely cured or much improved (these are often said to have "grown out of it"), and as many as one-third are completely free of attacks. Then there are women whose asthmatic attacks are predominantly premenstrual in a well-defined manner, and these attacks are completely relieved at the onset of the flow. Others have their attacks regularly during the flow, while some have attacks which appear haphazardly at any time during the month. Often patients are free from attacks during pregnancy—so much so that it has been alleged that attacks resembling asthma in the pregnant woman cannot be accepted as being genuinely asthmatic and should be regarded as hysterical (Curschmann, 1920). This freedom from an allergic manifestation during pregnancy is very similar to, and is probably on the same basis as, the temporary remissions of various skin allergies, hay-fever, and migraine; and of rheumatoid arthritis. At the menopause, again, some women are relieved, but others definitely deteriorate.

The endocrine basis of a certain proportion of cases of asthma in the female cannot be doubted—even less so nowadays when we learn that A.C.T.H. (Astwood *et al.*, 1950) and cortisone (Carryer *et al.*, 1950) can be used to relieve asthmatic attacks. The mechanism is not yet understood, but the result may be due to alteration in water, salt, or carbohydrate metabolism, or to modification of histamine and acetylcholine activity. Possibly also there may be some modification of neural mechanisms via the hypothalamus. Thus Introzzi and Larizza (1947) achieved good results in the treatment of bronchial asthma with folliculin, which they claim modifies the tonus of the vegetative nervous system.

Case Report

A. The Respiratory History

A girl first attended the London Chest Hospital in August, 1937, when aged 17. She gave a history of two weeks' dyspnoea of sudden onset, with sweating, wheeziness, and cough with purulent expectoration; the cough was troublesome by day, and the wheezing was cleared by coughing. Her dyspnoea was severe enough to necessitate her being propped up at night. Her only previous chest history was of an attack of bronchitis lasting two weeks when she was 14. She was small for her age and intelligent. Examination of the chest revealed numerous rhonchi scattered in both lungs, and crepitations at both bases. A radiograph of the chest showed the heart slightly deviated to the left, and the right lung field more radiolucent than the other. It was thought that the right lung was emphysematous, thus pushing the mediastinum over. Screening confirmed the appearance of pulmonary emphysema, the right dome moving little and being depressed and flattened. The heart was displaced to the left on expiration and became more central on inspiration. Mist. lobel. co. and ephedrine were given.

The patient was admitted for investigation. Bronchoscopy showed no abnormality; a right bronchogram revealed a normal bronchial tree, and the sputum was negative for tubercle bacilli. Bencard skin tests were negative for groups A1 and A2. She continued to complain of dyspnoea, which was not related to exertion, but came on many times daily while she was at rest. By June, 1938, she had improved considerably, but had a recent recurrence of dyspnoea, especially when she walked.

B. The Menstrual History

Meanwhile the patient had also been attending the London Hospital on account of the retarded development of secondary sex characters and failure to menstruate, and a report suggested that this delayed puberty was due to her poor general condition. She continued to attend right through the latter half of 1939 and the early part of 1940, with varying response to treatment. She was seen again in April, 1943, when it was reported that she had not worked for three years, that she had remained short of breath but had not been too bad until lately, and in addition had had a sharp pain and an intermittent dragging sensation on the left side. Examination showed that there had been no change in the general bodily size or contour. Physical signs of emphysema on the right and numerous rhonchi on the

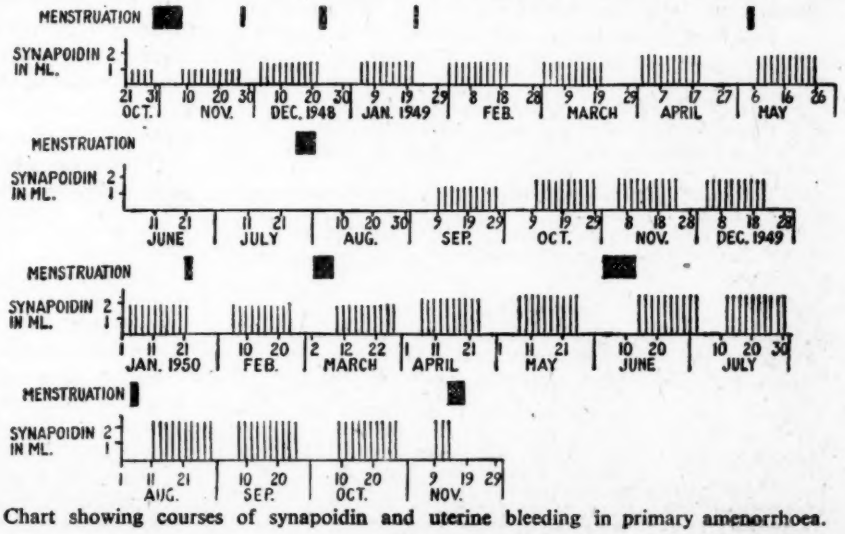

Chart showing courses of synapoidin and uterine bleeding in primary amenorrhoea.

left were found. An E.C.G. was of low voltage in Lead I, but otherwise the curves revealed no significant abnormality. Breathing exercises brought some benefit, but she relapsed in September, 1943. Rhinorrhoea and sneezing also developed. An E.N.T. report stated that she had the pale type of nasal mucosa often found in asthmatics. Nasal ephedrine drops considerably relieved her.

The patient was first seen by me in October, 1943, when she was 24. Her complaint was of severe asthma, and she had never menstruated. On examination she was pale and looked younger than her age. Her breasts were only slightly developed, being of the type generally seen in girls at the onset of puberty, and her external genitalia were infantile. There was no pubic hair and only slight axillary hair. Pelvic examination revealed an undeveloped cervix and a very small uterus.

The asthma continued unchanged in spite of all the usual palliatives, and in March, 1945, was severe enough to necessitate adrenaline injections. In September, 1945, stilboestrol, 0.5 mg. daily, was started, and by December, 1945, the patient was sufficiently improved to wish to start work. The daily stilboestrol was continued until December, 1947, when the dose was increased to 1 mg. daily. There was slight enlargement of her breasts.

In August, 1948, she was seen by Mr. Leonard Phillips, who advised a course of synapoidin. The size and spacing of the injections given is shown in the accompanying chart. The first 10 injections were followed by uterine haemorrhage lasting for eight days, the first menstrual period of the patient's life, at the age of 29.

By September, 1949, after eight courses of synapoidin and six periods, the cervix was definitely larger and softer and the uterus was a little larger. In April, 1950, the labia were quite normal and the uterus definitely larger. In October, 1950, the labia majora were fully developed and the labia minora were normal. The cervix was that of a normal adult, but the uterus was still small. The breasts were well developed, with prominent nipples and deeply pigmented areolae. A vaginal smear showed an adult type of keratinized epithelium. Treatment with synapoidin is continuing successfully.

The patient attended the London Chest Hospital for review in December, 1950, when she was able to report that she was much better than ever before, her breathing was easier, there was no cough or sputum, and instead of taking four or five ½-gr. (32-mg.) tablets of ephedrine daily she was now able to continue comfortably with two or three tablets a week.

Summary

A case of primary amenorrhoea with severe asthma is described. The use of endocrine therapy has resulted in the development of secondary sex characters and the establishhment of irregular menstruation, and simultaneously there has been considerable improvement of the asthma. Continued treatment may induce a true puberty with regular menstruation. As the patient is now 30 years old this may be very difficult, but the result so far has been most promising. Probably the improvement in the asthma is comparable to that noted in children at the time of puberty.

My thanks are due to Mr. Leonard Phillips for his advice and opinion; to Dr. N. Lloyd Rusby for giving me access to case notes at the London Chest Hospital; and to Dr. Martin Hynes for his encouragement and assistance with the microscopical examination.

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THE ALBUMIN ANTIBODY IN ROUTINE RHESUS GROUPING

ADAPTATION OF THE CHOWN CAPILLARY METHOD

BY

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Attention has been drawn in recent months to the difficulty experienced in maintaining adequate supplies to laboratories of Rhesus testing serum, especially anti-D. This difficulty has arisen from the increasing tendency to screen for this factor *all* expectant mothers and patients requiring blood transfusion. For these tests serum containing the complete or saline antibody is generally used, and the examination is carried out by the tube method. It is unfortunate that the blood of mothers of erythroblastotic infants usually shows a comparatively low titre of this antibody; more often the serum contains the incomplete or albumin antibody in high titre. It would appear that if this latter antibody were in general use the supply problem would be solved.

In the laboratory of the North Middlesex Hospital we found that the albumin antibody is suitable for routine screening, using the Chown capillary technique in which a saline suspension of the unknown red cells is allowed to fall through a column of serum containing the Rh antibody in a capillary tube. This tube is inclined at an angle of 45 degrees against an illuminated glass screen, the light source being so disposed as to give a fairly constant temperature of 37° C. across the screen face. The Rh-positive cells agglutinate into clumps which are readily seen with the naked eye, spaced in the length of the fluid with clear intervals between each, whilst the Rh-negative cells fall evenly to the bottom of the capillary type, leaving a clear supernatant fluid. This method combines the advantages of economy of serum and effort with rapidity, the positive results being apparent in 5–15 minutes, and it has been used exclusively in that laboratory since routine Rhesus screening was introduced in December, 1947, and from October, 1949, the albumin antibody has replaced the saline antibody formerly employed.

In the hands of some workers the Chown test seems to be a little difficult, but by rigidly adhering to the details of the technique as originally set out (Chown and Lewis 1946) no difficulty has been encountered by us and, furthermore, technicians become familiar with it after a few demonstrations.

To use the albumin antibody a few minor modifications of the original method have been evolved.

Apparatus.—The apparatus used is the box as described by Chown.

Capillary Tubes.—These are pulled from ordinary glass tubing similar to that used for making Pasteur pipettes. The internal capillary diameter should be about 0.5 mm. and the length about 8 cm.

Serum.—The serum containing the albumin antibody is diluted with an equal volume of 20% bovine albumin. Dilution with weaker albumin solution (15% or 10%) gives satisfactory results, but these take longer to appear, often 30–40 minutes, thus depriving the method of one of its advantages. The speed of the reaction is also affected by the titre, 1:8 being regarded as the lowest satisfactory for general use.

Such dextran solutions as have been available have proved unsatisfactory diluents owing to rouleaux formation.

Red Cells.—The unknown red cells, which may be obtained from either citrated or oxalated blood, or from the blood-stained serum of clotted blood after serum has been taken for Wassermann reaction or antibody investigation, are washed in saline and centrifuged at not more than 1,000 r.p.m. for three to five minutes. The supernatant fluid is withdrawn and the cells are resuspended in saline to approximately 40–50% concentration.

The Test

The test is carried out as described by Chown. The serum–albumin mixture is taken into a capillary tube for a distance of 2 cm. followed by the red-cell suspension for a distance of 0.5 cm. Care must be taken to avoid any intermediate air bubble. The capillary is then inverted and the lower end set in the plasticine bed at the base of the illuminated screen with the red cells uppermost so that they fall through the column of serum: agglutination is apparent in positive cases in 5–10 minutes; negative cases should be left 20 minutes before reporting.

Approximately 300 tests can be performed from 1 ml. of the original serum.

With this antibody the agglutinates tend to be larger than when the saline antibody is used, and they remain suspended in the fluid medium for at least an hour.

Results of Tests

Groups	Cases	Antibody Used	
		Saline (Dec., 1947–Sept., 1949)	Albumin (Oct., 1949–Mar., 1950)
Rh-positive ..	8,570	6,320	2,250
Rh-negative ..	2,024 (19·11%)	1,481 (18·98%)	543 (19·44%)
Total ..	10,594	7,801	2,793

All Rh-negative cases were checked by retesting when the first antibody assay was made or, in the case of blood donors, when the genotype was investigated. In the series of over 10,000 only 15 wrong groupings were found, proportionately divided between the two types of antibody used (saline 11 and albumin 4). No patient reported by us as Rh-positive has subsequently been shown to be Rh-negative.

Our cases were not in any way representative of a cross-section of the population, for the series included many expectant mothers referred to the antenatal clinics with obstetric histories suggestive of Rh incompatibility, most of whom proved to be Rh-negative. In maintaining the hospital blood bank the relatives of Rh-negative recipients also tended to increase the proportion of Rh-negative persons. Thus it is that our percentage of Rh-negative subjects is 19.11, against the figure of 16.8 given by Mollison, Mourant, and Race (1948).

Summary

A modification of the Chown capillary method for Rh grouping using the albumin antibody is described; the suspension of the unknown red cells is increased to 50% and the antiserum is diluted with an equal volume of 20% bovine albumin

The findings in a series of over 10,000 cases (7,801 tested with the saline antibody and 2,793 with the albumin antibody) are given for a comparison of results obtained by the use of these two antibodies; they are strictly comparable.

As the series included many cases referred to the laboratory for investigation a higher percentage of Rh-negative persons was found in our "population" than in a more representative cross-section.

I am indebted to Dr. J. F. Heggie for his help and encouragement in the preparation of this paper.

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Medical Memorandum

Rheumatoid Arthritis: Sustained Improvement on Low Dosage of Cortisone

A case of rheumatoid arthritis is presented which has been successfully treated for eight months with cortisone. After an initial period of treatment with high dosage, maintenance dosage has been reduced—gradually at first—to the lowest level short of provoking relapse.

Case Report

The patient, a boy aged 15, first noticed pain and swelling of the small joints of the fingers in January, 1950, while at his boarding-school. By the end of March, when his parents went to take him home for the holidays, they found him very lame with pain and swelling of recent origin affecting the left knee. He was also complaining of pain and swelling of the wrists and of the small joints of the fingers, so that he had difficulty in using his hands to feed himself.

He was put to bed at home on April 7, and a diagnosis of rheumatoid arthritis was made. The E.S.R. was raised to 90 mm. (Westergren) in one hour. He was given an initial intramuscular injection of 0.01 g. of sodium aurothiomalate and five subsequent weekly injections of 0.02 g. There was only slight improvement in his condition, and on June 24 he was admitted to hospital for treatment with cortisone. He then was afebrile, apart from an occasional temperature of 99° F. (37.2° C.). He was asthenic and of poor physique. His teeth and throat were healthy. His heart was normal. Glands and spleen were not enlarged. There was practically no movement in the right wrist. The left wrist could be flexed to 45 degrees, but there was no dorsiflexion. The wrist-joints were swollen, and attempts to move the wrists were very painful. The proximal interphalangeal joints of the hands were also swollen, and there was well-marked fusiform periarticular swelling of the left knee, with painful and restricted movement and wasting of the quadriceps (Fig. 1). A radiograph of the left knee

FIG. 1.—Photograph taken on June 28.

FIG. 2.—Photograph taken on July 28.

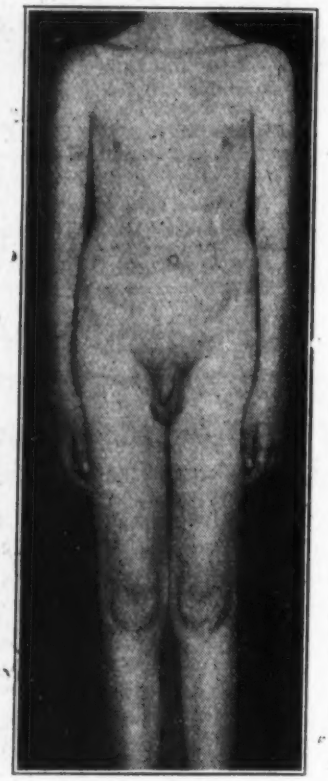

FIG. 3.—Photograph taken on September 4.

showed no changes apart from periarticular swelling, but radiographs of the hands revealed early changes of atrophic polyarticular arthritis. The E.S.R. was 50 mm. in one hour. A blood count showed: Hb, 78%; red cells, 5,100,000; C.I., 0.7; white cells, 15,000.

On June 28 treatment with intramuscular injections of cortisone was begun. He was given a total of 300 mg. daily for the first three days, by eight-hourly injections; then 200 mg. for two days, followed by 100 mg. for the next 10 days. Response to the drug was dramatic, as judged by the improvement in his general condition, increase in appetite, gain in weight, relief of pain, improvement in joint and muscle function, and fall in E.S.R. Side-effects did not occur. During this time he was kept on a low sodium diet, but had no other drugs except extra vitamins and codeine, at first, for relief of pain. After two weeks' treatment his weight had increased from 5 st. 1 lb. (32.2 kg.) to 6 st. 4 lb. (39.9 kg.) and the E.S.R. had fallen from 50 to 14 mm. in one hour.

Cortisone was then gradually reduced to the dosage shown in the Table. After the first two weeks of rest in bed in hospital, non-weight-bearing exercises were started for the legs, and exercises for the wrists and hands. After a month's treatment the swollen left knee-joint had practically returned to normal contour (Fig. 2), and there had been corresponding improvement in the function and deformity of the wrists and hands. He was allowed to get up and bear weight at the beginning of August, and on discharge from hospital on August 8 he was walking well, and had gained nearly 2 st. (12.7 kg.) in weight.

Date	Amount of Cortisone
June 28–30, 1950	300 mg. daily
July 1–2	200 ,, ,,
July 3–12	100 ,, ,,
July 13–20	50 ,, ,,
July 21–31	50 ,, on alternate days
August 1–September 3	50 ,, twice weekly
September 4–October 31	50 ,, weekly
November, 1950–February, 1951 ..	50 ,, fortnightly

His excellent progress continued, and by the beginning of September he was up and about all day and free from symptoms (Fig. 3). The deformity and limitation of movement of the affected joints had resolved. From September 4 he received a dose of 50 mg. of cortisone once a week, and was able to take up work as an apprentice in a factory. Since then he has kept well and has been regularly at work. The E.S.R. has remained normal. In November his maintenance dose was reduced to 50 mg. once a fortnight, and this dosage has been continued up to the time of writing (February, 1951) with the co-operation of his family doctor, Dr. J. W. P. Morgan, of Long Eaton.

Comment

In the original series of 14 patients with rheumatoid arthritis treated at the Mayo Clinic with cortisone (Hench *et al.*, 1949) all responded dramatically, but every patient except one relapsed when treatment was discontinued. Freyberg (1950) recorded 17 cases treated with cortisone with good results, which could be maintained with a dosage of 100 mg. three times a week. Goslings *et al.* (1950) reported five cases of rheumatoid arthritis treated with maintenance doses of A.C.T.H. for periods of two to six months. In this country, Copeman *et al.* (1950) recently confirmed the claims of the American workers and obtained a dramatic clinical response in five cases of rheumatoid arthritis treated with cortisone. Only a 10-day supply of the drug, however, was available for each patient.

Hench, in his recent lectures in Britain, has emphasized that the rebound relapse which follows the sudden withdrawal of cortisone can be averted by gradually tapering off the dosage. The present case is reported to illustrate the success of this technique. A supply of cortisone adequate for maintenance treatment was fortunately obtained from America as a gift from friends of the patient. The dose given is now so small that it would appear likely that cortisone could be discontinued without fear of relapse, but this is a risk which, so far, neither the patient nor his parents are prepared to face.

For the photographs, I am indebted to Mr. McLeod, clinical photographer, Nottingham General Hospital.

R. J. TWORT, M.D., M.R.C.P.,
Physician, Nottingham General Hospital.

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Some time ago the government of Land Niedersachsen passed a law making it compulsory for every inhabitant to undergo an *x*-ray examination for tuberculosis, and the first 500,000 *x*-ray examinations have now been completed. As this number includes individuals from the country, from small towns, and from the largest towns, the results may with justification be taken as applicable to West Germany as a whole. Tuberculosis not previously diagnosed was discovered in 1% of those examined, one in five of whom were found to be in need of active hospital treatment. It is estimated approximately three years will be needed to examine the whole population in Niedersachsen, when the cycle of examinations will be begun again. A yearly expenditure of 1,200,000 marks has been approved. In all six *x*-ray centres have been set up, with a total establishment of 90, among whom are nine doctors with special knowledge of lung diseases.

Reviews

ENZYMES

The Enzymes. Chemistry and Mechanism of Action. Edited by James B. Sumner and Karl Myrbäck. Volume 1. Part 1. (Pp. 724. $13.50.) 1950. Volume 1. Part 2. (Pp. 636. $12.80.) 1951. New York: Academic Press, Inc.

Multi-Enzyme Systems. By Malcolm Dixon, Ph.D., Sc.D., F.R.S. (Pp. 100. 7s. 6d.) Cambridge: At the University Press. 1949.

Thirty years or so ago the subject of enzymes was mainly considered in that section of a textbook of "chemical physiology" or of physiology which dealt with digestion. In other sections passing reference might be made to one or two intracellular enzymes, while a brief account would also be included of the experiments of Buchner (1897), in which the zymase was separated from yeast and shown to bring about alcoholic fermentation apart from living cells. Despite all this a generation or so ago the subject of enzymes was mainly a matter of digestive ferments.

At the end of the nineteenth century and during the early part of the present century many of the reactions which occur in biological systems and which we now regard as typically enzymic were thought to be vitally dependent upon the activities of the living cell. Pasteur had been one of many distinguished exponents of such a view, and it died hard. As late as 1927 we find a paper published in *Hoppe-Seyler's Zeitschrift* trying to explain away the significance of the results of Buchner and his followers. To those who retained such relics of a "vital force," alcoholic fermentation was the result of the activity of an "organized ferment" existing within the yeast cell and capable of acting only in the living system. Buchner's experiments were discredited in the eyes of such by the assumption that his separated yeast juice, active in promoting fermentation, must contain "expressed protoplasm."

From 1920 onwards Gowland Hopkins in this country, Warburg in Germany, and von Euler in Sweden, among others, began to lay with certainty the foundations of the view that separable intracellular enzymes provide the essential basis of all metabolic activity. Although some enzymes were found to withstand all attempts to bring them into aqueous solution, and in such instances enzyme activity was dependent upon the presence of insoluble elements of the cellular structure, such elements were in no sense living, and their insolubility was not of immediate relevance to the main question. Recently it has been found possible to bring many hitherto insoluble enzymes into solution by the use of butanol (R. K. Morton, *Nature, Lond.*, 1950, **166**, 1092), and no doubt many other previously intractable ones will yield to such treatment.

In 1926 Sumner in the U.S.A. crystallized urease from jackbean meal and showed it to be a protein. Since that time the view has become widely accepted that enzymes in general are protein in nature, although in many instances they require the presence of non-protein co-enzymes for their functional activity. It is now agreed that proteins possessing such enzymic activity constitute a large part of the living cell and that these enzymes are responsible for catalysing and generally controlling the metabolic processes which take place in it.

The two-volume treatise on enzymes edited by Sumner and Myrbäck, of which the two parts of the first volume have so far been published, is an encyclopaedic work. Each chapter has been prepared by an authority on the subject discussed, and although this makes for some unevenness a work provided by the co-operative efforts of 78 outstanding investigators drawn from the U.S.A., Canada, Europe, and Australia cannot fail to carry authority. In the first part of Volume 1 are included eight chapters on general questions such as the formation of enzymes, their role in adaptation, their cytological foundation, and their relation to other biologically active substances and to immunochemistry. These chapters also cover the physical chemistry of enzymes, the kinetics of enzyme reactions, and the inhibition of enzymes by chemical reagents. In the last chapters of the 19 in the first part of Volume 1 begins the systematic survey of all enzymes which can be said with any certainty to have individual existence and which are reasonably well known. This systematic survey is continued in Volume 1, Part 2, which begins with cellulases and related enzymes, and concludes with carbonic anhydrase. In most instances the references given in footnotes cover the ground adequately up to the last few years, but in Chapter 13, on sulphatase, there is only one reference later than 1938, and the whole chapter bears a striking resemblance to an earlier review by the author of this chapter. Nevertheless, for general reference this work as a whole is unequalled and invaluable, and we shall look forward to the second part of Volume 2 with eager expectation.

It is to be hoped that the time lag between the appearance of the two parts of Volume 2 will be somewhat less than that between the two parts of Volume 1, since the first part of Volume 1 contained no index, and its value was correspondingly diminished until the appearance of the second part of Volume 1. The present reviewer wonders why the term "enzymatic" has been so widely adopted in this work instead of the simpler, more euphonious, and much more directly derived word "enzymic." "Enzymes" surely lead to "enzymic" and no other word is needed; the derivation of "traumatic" from "trauma" is really not relevant, although it may be the reason for the introduction of the extra syllable in the word derived from "enzyme." The production of the two parts of Volume 1 is good, the diagrams and illustrations are clear, and the index is adequate. Undoubtedly the work will come to be accepted as a standard reference book in the course of time, although its price in England will deter many who might otherwise buy it, and whose need for it may be great.

While the treatise edited by Sumner and Myrbäck bears witness to the enormous accumulation of information about separated enzymes that has become available in recent years, Dr. Malcolm Dixon's little book, based on four special lectures delivered at University College, London, has a different aim. This is to set out in a succinct manner modern views on how intracellular enzymes may be considered to be coupled together functionally within the living cell, and to discuss some of the processes which such coupled systems promote. For the complex processes associated with living matter to proceed, a certain minimum number of enzymes must be bound together, functionally and perhaps morphologically, in a system that can bring about energy-yielding reactions. Such systems can then transfer this energy to other systems, where it can be used for many different processes. Dr. Dixon

discusses in particular two types of reactions of this type: the transfer of hydrogen, which generates energy, and the transfer of phosphoric acid groupings, which makes possible the utilization of stored energy for a multiplicity of purposes. The idea that enzymes work in "multi-enzyme" systems within the cell has been of most fruitful significance within recent years, and Dr. Dixon's account of this aspect of a vast field is a delightfully written one which will be easily understood by all those interested in the subject. Some of the material included is unpublished—for instance, that concerned with the concept of r P (phosphate pressure), but all the material, whether published or not, is presented in a new and interesting manner.

If the treatise of Sumner and Myrbäck can be regarded as a substantial main dish, then Dixon's volume is a delightful dessert. It is a pity that no references are included in the latter work, and its index is somewhat meagre. But it is a book for reading, and nobody interested in enzymes should miss it.

F. G. YOUNG.

ENCYCLOPAEDIA OF SURGERY

British Surgical Practice. Edited by Sir E. Rock Carling, F.R.C.S., F.R.C.P., and Sir James Paterson Ross, K.C.V.O., M.S., F.R.C.S. Volume 8. (Pp. 597; 264 figures. £3. Index £1.) London: Butterworth. 1950.

About two years ago we had the opportunity of reviewing very favourably the first two volumes of this work. The publication of six further volumes in the interval has now been completed by the issue of Vol. 8 (Spleen to Yaws). In a short notice it is impossible to deal with individual subjects critically, but there can be no doubt that more extensive acquaintance with the work has increased our admiration for this contribution to surgical literature. Since our review of the earlier volumes it has been possible to test the reference value of the information provided, as from time to time certain queries have arisen on many subjects in both the practice and the teaching of surgery. We can say without flattery that the work has stood up to this test excellently and that we have rarely failed to find the authoritative answer to our quest.

It has to be recognized that no encyclopaedia, even of eight volumes, can be expected to cover every aspect of a subject in as full a manner as a monograph, but many of the chapters surprise us by their completeness. The careful balance of the earlier volumes has been maintained throughout without neglecting short articles on such sidelines of surgery as compensation damages and pensions, the law in surgery, artificial limbs, electromyography, electrocardiography in surgery, and so on. An abundance of excellent illustrations continues to be a feature of the publication; some of the coloured ones deserve special praise for the truth of the reproduction—e.g., those in the sections on eye diseases, cystoscopy, and gastroscopy. It is unfortunate that the death of the author of the section on thoracoscopy (Mr. Tudor Edwards) has meant the omission of illustrations of this subject, since it lends itself so well to graphic teaching.

All subjects of any surgical importance seem to have been covered, as an examination of the Index Volume, of some 360 pages, discloses. In a book of encyclopaedic proportions the index volume is perhaps one of the most important parts of the production; there is no doubt that here this work has been well and fully carried out. Of the work as a whole it would be possible to make a few pettifogging criticisms, but to do so would throw into higher relief the generally high merit of the production. Proof reading has been good: there are very few printer's errors. The format is of a pleasing standard and the binding and finish fitting for a book which we feel will come to be recognized as one of the best of its type, a worthy representative of British surgical literature.

NORMAN C. LAKE.

THE ANKLE-JOINT

Injuries to the Ankle. By J. Grant Bonnin, M.B., B.S.(Melbourne), F.R.C.S. (Pp. 412; 399 figures. £3 3s.) London: William Heinemann Medical Books. 1950.

Mr. Bonnin is to be congratulated on his enterprising and stimulating account of ankle-joint injuries. For the most part the author's opinions, and his analyses of the mechanics of the various injuries, are readily acceptable, but some are provoking. The subdivision of first-degree external-rotation fractures of the external malleolus into three groups is unnecessarily elaborate, for the second and third groups are potential second-degree injuries and should be treated as such. In the treatment of sprains and fractures more emphasis might be laid on the need for functional activity and immobilization in plaster for an adequate period rather than on physiotherapy and procaine infiltrations. It is difficult to believe that there is anyone who would consider the use of leeches in the treatment of sprains, while few would agree that the operative treatment of complete ligamentous ruptures is often indicated. In the final chapter on operative treatment the reference to arthroplasty for ankylosis of the ankle might well be omitted in future editions. But in a monograph of this kind, expressing as it must the author's views on relatively common problems, it would be surprising for a reviewer not to find grounds for critical comment.

In all respects the book calls for praise, for it is of the right size, the work is well arranged, and the diagrams and radiographs are excellent. It undoubtedly fulfils a need, for a detailed study of ankle-joint injuries has not appeared before in English. It should be read by all those interested in the treatment of these injuries.

J. S. BATCHELOR.

IMPLICATIONS OF PSYCHO-ANALYSIS

Trends in Psycho-Analysis. By Marjorie Brierley. International Psycho-Analytical Library No. 39. (Pp. 320. £1 1s.) London: Hogarth Press. 1951.

With but a few outstanding exceptions the positive contributions of women analysts to psycho-analysis have been scanty, unimaginative, and, in exegetical respects, lacking in discipline or perspective. Dr. Brierley, whose reputation for careful evaluation is based on a broad scientific training and a happy flair for striking a balance, has in her present work added not only to her own stature but raised appreciably the low level of disciplined thinking which in recent years has seriously reduced the scientific standing of psycho-analysis in this country. Her book should not only be made part of the obligatory reading of every psycho-analytical student, but be studied with care by psychologists, sociologists, and humanists of whatever persuasion.

Her work falls naturally into two sections. The second, longer, and, from the general reader's point of view, more digestible part is concerned with the implica-

tions of psycho-analysis for human life and conduct, in particular the development of positive integrative values. This naturally calls for a preliminary survey of recent tendencies of psycho-analytic theory, which Dr. Brierley provides in the first part. In this connexion the author seems to have been not only stimulated but to some extent distracted by the violent controversies that for some time have rocked the British Psycho-analytical Society. She devotes a disproportionate amount of energy to the later theories of Melanie Klein regarding child psychology, and her criticisms, though pointed enough, are couched in an unnecessarily timid and apologetic form. The reason for this is apparent at various points throughout the book, where she appeals for an impartial approach to new ideas, an entirely laudable ideal which, she maintains, can be obtained only through the "training-analysis" of students. In only one brief sentence, however (in Chapter III), does she hint at the existence of a fatal flaw in this argument. It is notorious that the transference developed in course of training-analysis leads almost invariably to an uncritical tendency on the part of the student to accept and propagate his analyst's theories. The inevitable result is that the "validity" of these theories comes to depend as much on the counting of students' noses as on scientific evaluation. It is certainly true, as Dr. Brierley points out, that "to conserve the letter of all Freud's statements as a kind of Bible of Psycho-analysis is to condemn psycho-analytic inquiry to stasis, and, therefore, psycho-analysis as a science to death." On the other hand, psycho-analysis is less likely to be smothered to death by a careful adherence to basic principles than by developing a luxuriant overgrowth of untested and inherently improbable speculations that find a fertile soil in the mimetic minds of emotionally vulnerable candidates. There is, after all, such a thing as a scientific canon by which apocryphal ideas can be tested, but these tests cannot be successfully applied by acolytes; to which it may be added that the value even of non-partisan evidence depends on the contributor's scientific training and sense of judgment—qualifications which vary widely in the psycho-analytical field.

With the contention advanced in the second part of the book, that the attitude to life implicit in psycho-analysis constitutes a "neo-realistic humanism" which leads to "more enlightened, realistic, and integrative standards . . . relevant to the psycho-social necessities and the actual conditions of world affairs," readers will no doubt react with a degree of scepticism proportionate to their estimation of the "neo-realistic humanism" exhibited by such analysts as they have personally encountered. But they cannot deny the service Dr. Brierley has rendered in attempting to assess the integrative and redintegrative value of psycho-analysis in human adaptation, or the skill and erudition with which she brings her assessment in line with work in cognate fields.

EDWARD GLOVER.

TEXTBOOK FOR PHYSIOTHERAPISTS

A Textbook of Medical Conditions for Physiotherapists. By Joan E. Cash, B.A., M.C.S.P. With foreword by Frank D. Howitt, C.V.O., M.A., M.D., F.R.C.P. (Pp. 350; illustrated. £1.) London: Faber and Faber. 1951.

The title of this book is a little deceptive, for its contents embrace the practical application of physiotherapeutic procedures to diseases of various systems in addition to a description of these diseases. The author gives first an account of basic pathological response to disease, of circulatory disturbance, and of atrophy and hypertrophy. A large section is then devoted to an account of rheumatic conditions, and, although this is mostly on orthodox lines, it is a little startling to find gonococcal and tuberculous arthritis classified under the heading of "rheumatoid type of known causation." The section on non-articular rheumatism is well done, and it is of interest to note that in this book "fibrositis" is discussed with a moderation unusual in textbooks of physiotherapy. In an excellent section the author describes diseases of the respiratory system, which are now so extensively treated by physiotherapy. Sections on diseases of the nervous and cardiovascular systems are followed by one on diseases of the abdominal viscera and peritoneum, and it is perhaps in this section that the author is least happy.

The sections on the application of physiotherapy to disease are the work of an enthusiast in her own profession. This means that claims are made for the efficacy of various procedures which may have escaped the attention of the medical profession. These claims are on the whole made with fairness and moderation, and we welcome the author's forthright statements that in certain conditions—for instance, diseases of the heart—medical opinion does not usually support the use of physiotherapy. Some traditional unsubstantiated claims of physiotherapy are still perpetuated, and we are still told in the section on rheumatoid arthritis that "abdominal massage stimulates digestion, absorption and elimination," and this claim is repeated in the section on abdominal conditions.

This book will prove invaluable to students of physiotherapy, for the author approaches the subject from the point of view of orthodox medical thought rather than that of physiotherapeutic tradition.

WILLIAM TEGNER.

BOOKS RECEIVED

Review is not precluded by notice here of books recently received

The Further History of a Scottish Voluntary Hospital. By T. C. Mackenzie, M.D., F.R.C.P.Ed. (Pp. 144. 7s.) Inverness: The Royal Northern Infirmary. 1950.

Handbook of Tuberculosis Activities in Great Britain and the Commonwealth. Edited by H. Williams, M.D. 13th ed. (Pp. 370. 30s.) London: National Association for the Prevention of Tuberculosis. 1951.

Nitrous Oxide-Oxygen Anesthesia. By F. W. Clement, M.D. 3rd ed. (Pp. 369. 46s.) London: Henry Kimpton. 1951.

Clinical Parasitology. By C. F. Craig, M.D., M.A., Sc.D., F.A.C.S., F.A.C.P., D.S.M., and E. Carroll Faust, M.A., Ph.D. 5th ed. (Pp. 1,032. 84s.) London: Henry Kimpton. 1951.

Dental Surgery and Pathology (fourth edition; Staples Press; £3 3s.), by T. W. Widdowson and E. V. B. Widdowson, which includes special chapters by other authors, is intended as a work of reference for students and practitioners. An attempt is made to cover a very wide field, and it results in several inadequacies. In many sections there is little account of important modern work. Throughout there is a tendency to quote opinions of all sorts, even if these opinions have been shown to be incorrect. It would perhaps have been more advantageous in a book of this type to have given the current opinion, or conclusions which have been reached, with a list of references from which further information could be gleaned where desired. Notwithstanding these slight deficiencies the book will undoubtedly be of considerable value both to students and to practitioners.

BRITISH MEDICAL JOURNAL

LONDON

SATURDAY JUNE 30 1951

CONTROL OF WHOOPING-COUGH

Six years ago McFarlan, Topley, and Fisher[1] reported in this *Journal* the failure of a whooping-cough vaccine to control the incidence and severity of this infection in groups of children attending welfare clinics and day nurseries, or living in residential nurseries, in the city of Oxford. In an editorial comment we suggested that before steps were taken officially or unofficially to extend the practice of vaccination against whooping-cough further observations should be carried out under the most carefully controlled conditions to determine the value of this procedure. By this time plans had already been formulated by the Whooping-cough Immunization Committee of the Medical Research Council for extensive field trials of different vaccines; in particular it was felt desirable to test the vaccines used by Sauer and Kendrick, which had apparently proved their worth in the U.S.A. The first of these trials, with the Sauer vaccine prepared by Parke Davis and Co., Detroit, was begun in Oxford in 1944, and the experience gained in this investigation was of value in the organization of a further series of ten separate trials in five areas—Manchester, Wembley, Tottenham and Edmonton, Leeds, and West Ham. The material consisted of five batches of vaccine from three manufacturers—two American (the Sauer vaccine and the Kendrick vaccine from the Michigan State Laboratories) and one British (an alum-precipitated vaccine from the Glaxo Laboratories). In all these trials, reported in detail in the opening pages of this issue, an anti-catarrhal vaccine which was not expected to give any specific protection against pertussis was used for inoculation of the children in the control groups. The children included in the trials came from families whose parents voluntarily agreed to have their children inoculated, in the knowledge that some of the children would be given the anti-catarrhal vaccine and that in any case no guarantee of protection following the inoculations could be given. In each area the trials were organized through the public health department with the enthusiastic support of the medical officer of health and his staff, some of whom, as medical officers and health visitors, were actively engaged in the field work throughout the three to four years that elapsed before the investigations in any area were completed. Dr. W. C. Cockburn, of the Public Health Laboratory Service, was responsible for the general organization and direction of these studies, and it is a great tribute to the team spirit which was engendered that similar investigations have been going on continuously in some of the areas since 1945.

In any controlled investigation into the prophylactic or therapeutic value of an agent it is most desirable that the two groups, treated and control, should be as similar as possible and that those engaged in the conduct of the trials should not know whether any particular individual belongs to the treated or control group. These tenets were admirably fulfilled in the present trials, and, indeed, the resemblance of the control to the treated group was almost uncanny. Thus, besides the similarity in age and sex, the proportion and duration of breast-feeding, the incidence of other infectious diseases, and the percentage in each group which had been vaccinated or immunized against diphtheria were remarkably alike. It may be noted that the figures for breast-feeding and vaccination among the children in these trials are well above the average rates for the country generally, and therefore these volunteer children are not necessarily a representative cross-section of the child community. The important point is that for the purpose of assessing the efficacy of the vaccine the two groups are closely comparable with each other. Another desideratum, that the medicament be safe as well as effective, was also satisfied, for with the exception of a few sterile abscesses with the alum-precipitated vaccine there were no serious local or systemic reactions following the inoculations. It is also satisfactory to note that despite careful scrutiny of the records of all vaccinated children no cases of convulsions or encephalopathy (which have caused some concern in the U.S.A.) were noted in the present large series, nor was there any case of post-inoculation poliomyelitis, though the vaccines were mostly given intramuscularly and in at least two areas at a time when poliomyelitis was epidemic.

The children taking part in the trials were seen at monthly visits for two years or more after the last inoculation, and any child with a suspicious cough was specially visited and pernasal swabs taken for bacteriological examination. This must have meant the culture on Bordet-Gengou medium of many thousands of swabs, and it is very creditable that some 60% of the clinically diagnosed cases were also positive bacteriologically. When a case of whooping-cough was confirmed an assessment of the severity

[1] *British Medical Journal*, 1945, **2**, 205.

and duration of the attack was made. The overall analysis of incidence and severity of attack in the two groups showed a very significant advantage to the vaccinated children. It is particularly noteworthy that among children intimately exposed to infection by a sibling in the family, which gives a secondary attack rate around 90% in unprotected children, the ratio in favour of the vaccinated children was about 5 : 1. Incidentally, less than one-quarter of all the affected children acquired whooping-cough in this way, and in about half the cases there was no history of exposure. Equally important was the modification of severity in the vaccinated group, of whom 73.2% had mild attacks compared with 24.1% in the control group. Whooping-cough is so often a protracted and debilitating infection in children of this young age that a vaccine which attenuates and shortens the infection, even if it does not completely protect, is surely worth while, and the modified attack, provided the child suffers no ill-effects, may have some advantage in inducing a more lasting immunity than the vaccine alone can procure. In these trials, however, the immunity induced by vaccination showed no tendency to wane over the period of two years or more of the follow-up.

When the results obtained with the three vaccines were analysed separately, the Kendrick vaccine gave considerably greater protection than the other two vaccines—for example, the attack rate for home exposures was more than 10 : 1 in favour of the vaccinated child, compared with ratios of 4 : 1 and 3 : 1 for the Sauer and Glaxo vaccines. What factors in the nature and preparation of the Kendrick vaccine are responsible for this superiority cannot at present be defined, but the results vindicate the missionary zeal which Dr. Pearl Kendrick and her colleagues have shown over the past 15 years for prophylactic vaccination against whooping-cough, and it is encouraging to know that British vaccines made to the Kendrick formula are at present on trial by the Whooping-cough Immunization Committee.

What is particularly needed now is some laboratory yardstick which will differentiate between good and poor vaccines. Some progress has already been made in this direction in the U.S.A. by means of a mouse-protection test. The problem of large-scale production is also being met there by increasing use of vaccines prepared in liquid media. For convenience in administration these vaccines are being combined with diphtheria toxoid and, in some instances, tetanus toxoid as well. The age at which to vaccinate and the number of injections are still matters for argument, but these carefully controlled trials should convince the sceptics that prophylactic vaccine against whooping-cough can be both safe and effective, and should lead to its much wider use in this country. To hope that some of the new antibiotic drugs will obviate the need for preventive measures is foolish, for often whooping-cough may not be diagnosed before much harm is already done to the patient. In a disease of such prevalence and severity prevention must always be better than cure.

METHODS OF MEDICAL TEACHING

In the educational number of the *Journal* two years ago we published a symposium of articles on the teaching of the basic sciences in medicine, and as a sort of addendum to this included an article by a professor of education on the training of the teacher. Commenting on this we observed that it was unusual "to find so plainly stated the need to improve the teachers as well as the taught and the teaching." This was not a novel idea, as it had been suggested by Dr. Ffrangcon Roberts in 1944.[1] The interest aroused in this hint that those who teach students should take some thought about their methods and techniques prompted us to publish in the educational number last year a symposium of articles on educational methods in medicine. The Royal College of Physicians has recently set up a committee on the teaching of teachers, and the Postgraduate Medical School of London held a two-day course last week, the attendance at which was a most welcome illustration that those who now teach medical students are free from self-complacency about their approach to this highly important problem. A report of this course elsewhere in this week's *Journal* will give the reader some idea of the drift of the debate.

In the *Journal* symposium last year, Professor Lauwerys[2] did not favour any systematic instruction of the university teacher in his task, but suggested that it would be an advantage if departmental heads were to discuss at regular conferences with their staff educational and pedagogical problems; and in a sense this was the model followed by the Postgraduate Medical School last week. Both the teacher and the taught unfortunately cannot escape the spectre of the examination hall. Students (and their parents) see in the inevitable examinations a series of obstacles between them and the responsible exercise of their profession as independent men and women. The student goes to the examination feeling heavily burdened with facts and anxious lest the examiner should find him deficient in a few out of many thousand. Obviously there must be a minimum of knowledge of facts without which it is not safe to let

[1] *British Medical Journal*, 1944, 1, 728.
[2] Ibid., 1950, 2, 471.
[3] Ibid., 1949, 2, 526.

loose upon the public one who wishes to practise as a doctor, but the bogy of the examination compels the student to see in medical education a painful exercise in cramming rather than an instruction in method and principle and a process which should bring out those qualities indispensable to the good doctor. This demand of the student is bound to have an effect upon those who teach him, and establishes the reputation of those in our medical schools who can almost guarantee to get the dullest dog through the conjoint or other similar qualifying examination. One way to counteract this tendency, as Sir Francis Fraser hinted last week, is to imbue all medical teaching with the university ideal, the university being a community of teachers and students. That this ideal is in danger of being ignored was suggested by Professor Ernest Finch's remark that he found men applying for surgical posts who regarded themselves "purely as surgical technicians," and he deplored what he saw as a tendency to produce a breed of "slick operators." The word "university" suggests remoteness from the practical side of life, and the history of medicine shows how this tendency to remoteness has been corrected by those who may be said to represent the art and craft of medicine and surgery. The influence of the Royal Colleges has been paramount in this respect. Yet, with the present flood of specialized techniques, the spirit of the university is more than ever necessary in medical education.

Perhaps the most bewildering phase of the medical student's life is when he passes from his preclinical studies to the out-patient department and the wards of a teaching hospital. Here, for the first time, he is confronted with facts that do not fit neatly and conveniently into some theoretical structure. Physiology and anatomy appear to him as disciplines but remotely connected with the aches and pains of the patients. The educational experiment described by Professor Robert Platt is therefore of much interest. During the past two or three years there have been held at the Manchester Royal Infirmary clinico-pathological discussions for students taking physiology. These are conducted by a lecturer, the professor of physiology, and the professor of medicine; in this way the student is shown how his education is a continuous process and not a series of isolated and disconnected mental exercises. When the student goes to hospital he often sees himself as someone who, for two or three years, will be "walking the wards," and Professor G. W. Pickering is right to stress what has been so characteristic of British medical education, the teaching at the bedside. But perhaps there is need to bring the out-patient department more to the forefront of hospital teaching. As Mr. A. J. Gardham points out, one of the great advantages of this department for the student is that there he witnesses the teacher's mind continually at work on fresh problems. Immediate decisions have to be taken; the cases are not selected; textbook pictures are rare; the possibility of error exists, and this should not be concealed from the student. Certainly the experience in the out-patient department is much closer to the experience of general practice, and one more representative of the ailments of humanity than that which is obtained by examination of selected cases in the wards. The two kinds of experience are, of course, complementary, but the student should perhaps be put on his guard against the intellectual attractions of the exhaustively investigated patients lying in hospital beds.

Most of the men and women who attend our medical schools are destined to practise their profession as general practitioners or consultants, and, this being so, the aim must be at each stage to inculcate a sense of responsibility. As Professor Pickering observes, the student wants not only to know how to observe facts, but also how to interpret them. More than that, he wants to feel that he is a responsible member of the team and that, to some extent, the patient is being helped by the work he is doing. He wants to be brought more into what Professor Lauwerys described as "activity methods." It is, therefore, discouraging to find someone with the wide experience of Sir James Paterson Ross coming to the conclusion that "one of the most regrettable changes in practical medical education during the last thirty years was the disappearance of any sense of responsibility from the student." In his hospital it had become the rule that no student should on his own responsibility send a patient away, however trivial the condition. The reasons for this are evident, but this tendency cannot be without its ill-effect upon the student. If the student is not to be allowed to take more and more responsibility as he goes through hospital, he will be so much the less fitted to practise medicine to the benefit of his patients when he qualifies.

The Postgraduate Medical School has done a signal service in holding the conference course on medical teaching, and it is to be hoped that the success of this experiment will encourage further efforts in this direction. It appears that no educationist took part in the conference, and it would be worth considering whether such a conference between teachers of medicine and teachers of teachers would not carry the debate a stage further. As Professor W. R. Niblett suggested in these columns two years ago,[3] much might come out of co-operation between institutes of education and schools of medicine.

CORONARY ARTERY DISEASE

Physicians find little agreement among themselves about the correct title for a prolonged attack of cardiac ischaemic pain. "Coronary thrombosis" is hallowed by long usage but is inaccurate, for coronary thrombosis is not present in all cases of myocardial infarction, and a coronary vessel may be occluded by arteriosclerotic changes but not thrombosed. "Myocardial infarction" is no better, because more than four-fifths of 950 men who died from coronary artery disease failed to show an infarct at necropsy.[1] Perhaps "coronary occlusion" is a more precise term than any other, although death may occur from cardiac ischaemia with patent coronary arteries. In these cases spasm may occlude the vessel long enough to produce an infarct, as Laubry and Soulié[2] have implied. Fortunately none of the commonly used terms is likely to be misunderstood.

There is a form of coronary artery disease characterized by pain, typically ischaemic in quality but of longer duration than angina pectoris, yet lacking the usual associations of myocardial infarction—such as fever, leucocytosis, and increased erythrocyte sedimentation rate. The electrocardiographic changes of myocardial infarction do not develop, although fairly characteristic ST segment abnormalities are the rule. This syndrome bears no definitive name; it is known by a variety of titles, including "acute coronary insufficiency" and "coronary failure." Drs. C. Papp and K. Shirley Smith[3] used the term "slight coronary attack" to include this and other forms of atypical cardiac ischaemic pain. The survival of the patient may depend on the early recognition of this form of coronary insufficiency, for it is often the forerunner of myocardial infarction. Prompt administration of anticoagulants combined with complete bed rest may avert the danger. The eventual course of such an illness is not easy to predict, but a favourable response to treatment when the symptoms are acute and alarming warrants a hopeful outlook.[4]

Elsewhere in this issue of the *Journal* Papp and Shirley Smith have attempted to assess the prognosis of myocardial infarction according to three degrees of severity—slight, moderate, and severe. The terms are useful provided their limitations are understood. In the group of "slight cardiac infarction," pain, often prolonged but not severe, was the main clinical feature—cardiac failure and severe shock being absent. Yet such a clinical picture, presenting as a not alarming illness, may usher in sudden and unexpected death, as Yater and his colleagues[1] have shown. We recently emphasized the importance of bearing in mind the variants from the natural course of myocardial infarction in any discussion on mortality.[5] Assessment of prognosis raises similar problems. The unfavourable portent of untreated severe shock and cardiac failure is beyond question. The majority of the fatalities in Papp and Shirley Smith's series (39 out of 50) were so complicated, and they conclude that anticoagulant therapy should be reserved for this type of case. In their opinion the outlook in "slight" cases, with pain alone or with slight shock in addition and electrocardiographic evidence of infarction, is so hopeful (less than 9% mortality over an observation period of four years) that anticoagulant therapy is unwarranted. But the physician confronted with a patient complaining of cardiac pain for 6–8 hours but without shock or failure may now find himself in a quandary: can he withhold anticoagulants with safety because, according to the current definition, the patient has only a "slight" myocardial infarction? An affirmative answer would be hard to defend in the light of the uncertainty of early prognosis referred to earlier. It seems that the only way such a problem can be solved is by long-term observations on a large number of controlled cases. Small series often disclose a trend which may be confirmed or overthrown when experience is wider.

The clinical picture and pathological findings in 950 fatal cases of coronary artery disease in males of different ages, from 18 to 50 years and over, have been compared and reviewed from a different aspect by Yater and his co-workers.[1] They found that fatal attacks are more likely to occur without warning in men under 40 years of age, and that the survival period after the acute attack tends to lengthen as age increases. The incidence of pain, 98% in the younger group, decreased to 84% with advancing age, though collapse occurred more often in men under 40 than in those over 40. Painless myocardial infarction has always been a controversial subject: in Yater's series patients without pain tended to live longer than those with painful infarcts. In men under 30 the infarcts were usually in the anterior wall of the left ventricle, but posterior infarcts were found more often as age increased. Five years ago Moritz and Zamcheck[6] cast doubt on the widely held opinion that men under 40 with myocardial infarction were usually overweight or of a stocky build: they were able to show that the weights of such patients did not differ from those in the same age group dying from traffic accidents or accidental gunshot wounds. Similarly, Yater and his co-workers could find no

[1] Yater, W. M., Welsh, P. P., Stapleton, J. F., and Clark, M. L., *Ann. Intern. Med.*, 1951, **34**, 352.
[2] *Les maladies des coronaires*, 1950, Paris.
[3] *Brit. Heart J.*, 1951, **13**, 17.
[4] Wood, P., *Diseases of the Heart and Circulation*, 1950, London.
[5] *British Medical Journal*, 1950, **2**, 991.
[6] *Arch. Path.*, 1946, **42**, 459.

conclusive evidence linking obesity and myocardial infarction in men under 40. In men over 50, however, obesity is decidedly more common in those with, than in those without, myocardial infarction.

OEDEMA AND SALT

The importance of a diet of low sodium content in the treatment of congestive heart failure has been recognized for over half a century. As early as 1901 French clinicians were aware that patients in heart failure excreted chlorides poorly, and that retention of sodium chloride was an important factor in the development of oedema.[1-3] With the introduction within the last two decades of the organic mercurial diuretics—modern versions of the famous Guy's pill—there developed a tendency to regard control of fluid intake rather than sodium restriction as the factor of greater importance in the management of heart failure. Some clinicians were inclined to regard the organic mercurials more as eliminators of water than of sodium. But in fact these mercury compounds exert their chief action by decreasing tubular reabsorption of sodium, increased secretion of urine being a direct osmotic consequence of decreased sodium reabsorption by the kidney. During the past 10 years, largely because of American research, the importance of the sodium ion in the disturbed haemodynamics of congestive heart failure has again come to the fore. Perhaps the most important early contribution to this topic was Schroeder's[4] demonstration that in heart failure ingestion of sodium chloride in amounts below that excreted by the urine invariably led to decrease in oedema. Futcher and Schroeder[5] later showed that patients convalescent from congestive heart failure were able to excrete an amount of sodium chloride equivalent to only 30% of that found in normal controls. Proger and his colleagues[6] also demonstrated that oral administration of excessive amounts of salt to patients recently recovered from congestive heart failure led to abnormal retention of sodium, together with recurrence of symptoms and oedema. More recent studies with radioactive sodium[7 8] have confirmed these findings.

In the *Journal* of June 16 (p. 1349) Drs. A. L. Neilsen, P. Bechgaard, and H. O. Bang, from Copenhagen, gave further practical proof of the value of sodium restriction in the treatment of heart failure by recording the results obtained in 64 cases. These were convincing, particularly in four patients who proved resistant to rest, digitalis, and mercurial diuretics, but who improved greatly when the salt intake was reduced to less than 1 g. a day. Using increase in weight as a measure of progressive oedema, either occult or overt, the authors found that decrease in urinary salt excretion ran roughly parallel with weight gain, and that disappearance of oedema was matched by a corresponding increase in sodium chloride excretion. Their follow-up studies of convalescent patients suggest that the prognosis is more favourable in patients who maintain a low salt intake than in those who resume a normal diet. A longer period of observation of a greater number of patients will be necessary to establish this important point: only when clearer evidence is forthcoming will doctors generally feel justified in prescribing drastic salt restriction during convalescence from heart failure—a form of treatment which from the patient's point of view can be described only as weary, stale, flat, and perhaps unprofitable.

Rigid restriction to less than 1 g. of sodium chloride a day is essential in patients who fail to respond to rest, digitalis, and diuretics, and in whom the valuable but much-neglected treatment of acupuncture fails to break a vicious circle. It is doubtful, however, whether such rigid control is necessary or desirable in those patients who continue to respond well to mercurial injections. For them a diet which omits foods of high salt content and to which no salt is added in preparation or at the table will reduce the salt intake to approximately 2 g. a day: few patients will adhere faithfully for long to a diet containing much less than this, particularly when they are convalescent and feeling relatively well. Palatable food is one of the few pleasures remaining to many of these people, and the decision to prescribe a strict salt-poor diet for life (to which few doctors would submit themselves after once giving it a trial) should not be undertaken lightly. A further disadvantage of rigid sodium chloride restriction is the occasional development of the so-called salt-depletion syndrome. This is seen especially in elderly patients, in whom the limitation of salt and fluids, together with loss of these substances from mercury diuresis, may lead to anorexia, muscle cramps, weakness, and perhaps serious mental disorder. These symptoms are unlikely to develop in patients whose salt intake is not less than 2 g. a day and who receive only one or two injections of mercurial diuretics a week. Such a regime will keep the majority of ambulant cardiac patients relatively comfortable and oedema-free. Although not ideal it is a practical form of treatment which gives good results and is appreciated by the patient. If it fails, then the patient should be in hospital.

It is to be hoped that the intensive research now taking place on cation exchange resins may soon lead to the production of highly active substances capable of diverting via the gut considerable quantities of dietary sodium without hazard to the patient. A recent report by Dock and Frank[9] indicates that the most reliable two- or three-to-one mixture of ammonium and potassium resins will exchange only 1 mEq sodium per gramme of resin when the diet is normal. On a low sodium intake the exchange is even less than this. This means that a patient must somehow swallow several ounces of tasteless sand-like material to divert 1 g. of dietary sodium. But perhaps in the near future the diet kitchen may have more potent exchange resins to work on, so that such impositions as are placed upon the oedematous patient will be not only therapeutically effective but tolerable and even gratifying.

1 *C. R. Soc. Biol., Paris*, 1901, **53**, 346.
2 *Bull. Soc. Méd. Paris*, 1903, **20**, 678.
3 Ibid., 1903, **20**, 725.
4 *Amer. Heart J.*, 1941, **22**, 141.
5 *Amer. J. med. Sci.*, 1942, **204**, 52.
6 *Amer. Heart J.*, 1942, **23**, 555.
7 *J. Lab. clin. Med.*, 1947, **32**, 1169.
8 *Proc. Soc. exp. Biol. N.Y.*, 1947, **66**, 369.
9 *Amer. Heart J.*, 1950, **40**, 638.

SALMONELLA IN SEWAGE

The epidemiologist in search of the source of sporadic cases of enteric fever is sometimes able to show that infection was conveyed by water from a sewage-polluted river or stream. Efforts to trace the infection back to its source have in the past met with little success because of the difficulty of isolating the organism from the highly diluted sewage, in which it is greatly outnumbered by other bacteria, and because the pathogen may be present only intermittently. The first difficulty has largely been overcome by the use of the modern highly selective fluid and solid culture media for enrichment and plating. The other problem has been solved by Moore,[1 2] who has successfully devised a method for the isolation of enteric bacilli from sewage systems. The method consists in lowering folded pads of gauze through the manholes and tethering them with string so that they dip into the flowing sewage. Two to seven days later the pads are transferred to selenite F medium, from which, after overnight incubation, subcultures are made on selective solid media. For *Salm. paratyphi B* simple enrichment followed by plating on deoxycholate citrate medium gives good results, but for *Salm. typhi* it is better to make three successive tenfold dilutions in selenite of the original sample and plate them, after incubation, on deoxycholate and on Wilson and Blair's media. Moore has given a number of instances of the value of these aids to detective work, and the latest example is contained in a report by Lendon and Mackenzie.[3] These workers describe the investigation of a number of sporadic cases of typhoid fever in children who had drunk water from a stream in Hampshire. Typhoid bacilli were isolated from this stream, which was subject to intermittent pollution with crude sewage discharging through overflow pipes designed to carry away excessive storm water. Infection was then traced back through the main sewers of a residential area to the sewer serving a row of houses, and ultimately to a single house, in which a chronic carrier of typhoid bacilli was found. It was thought that this carrier, who had no definite history of typhoid fever, might have been infected some 60 years previously. An essential part of these investigations is the typing of the bacilli by specific Vi-bacteriophages.

1 *Mon. Bull. Min. Hlth*, 1948, **7**, 241.
2 Ibid., 1950, **9**, 72.
3 Ibid., 1951, **10**, 23.

UNIVERSITY CELEBRATIONS

Academic celebrations have lately added colour and warmth to this Festival summer in two northern cities. The highlight of the centenary of Manchester's Owens College—later to become Manchester University—was the Queen's visit on May 31 to receive the honorary degree of Doctor of Laws. Speaking of the development of the University, the Queen said that Lancashire had not only exported textiles to the world: it had exported ideas. One of the ideas of which the Queen spoke was the conception of a civic university, which probably did more than anything else in the last century to enlarge the scope of academic education in Britain. Though a civic university must by its nature have particularly close ties with the district in which it is situated, it is true of Manchester University, as the town's own great newspaper put it, that "it has endeavoured to meet not only the technically industrial requirements of its region but also its human, moral, or economico-moral needs.[1]

Manchester University may be said to have come of age. Glasgow University, whose quincentenary we have already welcomed,[2] has now reached full maturity. Last week in Glasgow, representatives from universities in this country, from Europe, from the Commonwealth, and from America took part in a series of ceremonies marked by a dignity and friendliness which should be the envy of all politicians. At the gathering in the Bute Hall on June 19 the Chancellor of the University, Lord Boyd-Orr, was presented with more than 150 addresses. The Principal, Sir Hector Hetherington, said they would cherish these memorials of good will. He continued: "The universities the world over have been, and surely will be again, a unity of diversities, working in fruitful interchange, each in the full vigour of its individual life, but all in faithful allegiance to the same ideals, upheld by the same imperishable hope." At the honorary graduation ceremony on June 20 there were many well-known medical men from all over the world among those who received the degree of Doctor of Laws. Of the two women who were thus honoured, one was Professor Dorothy Russell, the other Miss Freya Stark. The celebrations came to an end on June 21, when the Prime Minister addressed a gathering in St. Andrew's Hall.

1 *The Manchester Guardian*, May 25, 1951.
2 *British Medical Journal*, 1951, **1**, 81.

FESTIVAL OCCASIONS

The Festival Lecture,[3] delivered on June 20 by Sir Henry Dale, O.M., F.R.S., was one of two recreational occasions held during the Festival Scientific Meetings jointly organized by the Royal Society of Medicine and the British Medical Association. After being introduced by Lord Webb-Johnson, who was in the chair, Sir Henry delighted a large audience with his account of "Medicine Yesterday and To-morrow." He described the transformation of medicine in the last 100 years and the effect it had had on saving life and relieving suffering, leading up to the need to-day for bringing the new resources of medical knowledge to the individual patient and the community. Mr. Gerald Barry, Director of the Festival of Britain, thanked the speaker and drew attention to the Scientific Meetings as an important feature of the Festival.

Next day in the evening the President of the B.M.A. and the Chairman of Council, together with Mrs. Sichel and Miss Gregg, received about 250 guests at B.M.A. House. Mr. Marquand, the Minister of Health, was able to be there and spoke to the assembled company. After welcoming the presence of Dr. Sichel as a representative from South Africa "of your great profession," he contrasted the confidence of 1851 with the confusion of 1951, but set against that the remarkable increase in health and of the expectation of life. Dr. Gregg felicitously replied.

3 To be published next week in this *Journal*.

REFRESHER COURSE FOR GENERAL PRACTITIONERS

THE EARLY DIAGNOSIS OF SCHIZOPHRENIA

BY

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Psychiatrist to the London Hospital

Few doctors would have trouble in accurately diagnosing a full blown schizophrenia; all doctors, including specialists, make mistakes about early cases. This paper will largely exclude those cases marked by delusions and hallucinations where clear deviation of behaviour points to a psychotic process.

A diagnosis of schizophrenia is always a serious one, but the hope that came when Bleuler suggested the substitution of the term "schizophrenia" for dementia praecox still blows through psychiatry, and the encouraging results of some modern treatments have confirmed a moderate optimism, provided early diagnosis is made.

Acute Schizophrenic Reactions

During the war it was found that some apparently acute schizophrenic reactions which occurred in battle areas in exhausted soldiers would persist so long as the men remained in the foreign theatre of war, but would cease dramatically on return to this country. These cases show how schizophrenia may apparently come on after stress, and also how the condition may remit. No one seeing such cases would call them "hysterical," though the outcome might suggest this diagnosis. They are mentioned here as examples of the acute schizophrenic reaction, with marked hallucinations and delusions, which is akin to delirious reactions and in which the prognosis seems relatively good.

Such cases had been distinguished by Langfeldt before 1939, and have since been given the dysphonic name "oneirophrenia." Stromgen found that the heredity in 77 cases of this type was quite different from that in what has been called "process-schizophrenia." Their family histories should have yielded ten cases of indubitable schizophrenia and ten of doubtful schizophrenia; in fact, they yielded only one case in which the disease was indubitable, but many cases of neurosis and psychopathy.

These acute cases always need immediate segregation, but we shall largely concentrate upon a description of those types of schizophrenia characterized by introversion, day-dreaming, and less florid behaviour disorders.

Adolescence and Schizophrenia

The cardinal symptom in established schizophrenia is disordered thought. The fundamental attitude is that the external world is threatening, damaging, mischievous. The self is altered, but not responsible; for this outside agencies are blamed. The patient speculates about the alteration in himself and defends himself against this change in a number of ways that may give the impression of being neurotic. It is wrong to think that the patient is not profoundly upset emotionally at the beginning. In the later stages, affect is lost or incongruous, but a diagnosis should be attempted before such signs of an encrusted process are clamant.

Since three-quarters of the cases of schizophrenia begin between the ages of 15 and 30, they occur when the normal person is leaving the stage of dependency for one of responsibility. Some of the difficulties in diagnosis arise for that very reason.

Myerson has described the scrutiny and derision reactions in normal adolescents and has emphasized the difficulties that even normal youths experience in the presence of others, the apprehension they feel and the suspicious attitudes they may adopt. The most shy are those who are trying most to please others. Normal adolescents may be likened to crustaceans with some carapace, but with multitudes of antennae. Their experience is limited, yet they dare not admit this. They therefore brag, become ashamed, feel frustrated, give up in despair, or seek to solve their problems by ill-directed outbursts. Few if any children go through these years without showing temporary seclusiveness. Aims have a vacillating strangeness. Attachments, deep one moment, become shattered the next, and the youngsters appear illogical, fretful, morose and unpredictable to their elders. They are suspicious of secrets or the unmatured plans of others, and believe that they are being watched or checked when no such intent is admitted by their seniors.

The schizophrenic is incompletely equipped to cross the bridge between childhood and maturity. He uses time to think and day-dream. He develops fantasies about himself, at which his later bearing of superciliousness plainly hints, or he ruminates about normal bodily sensations until these merit the description of hypochondriacal delusions, which gradually become more and more bizarre. Lonely and sensitive, he becomes suspicious when workmates talk—it *must* be about him—or if they seem indifferent to him it is because he smells or has been miraculously deformed by secret agents.

Most of us dispel our parents' alarm, but many normal adults have shown during adolescence brief episodes of emotional instability. These can be reckoned as means of defence against the new perceptions and needs of these years. Few of us could assert that we had not felt unduly suspicious. There were periods when we secretly became hypochondriacal, we were not far from developing a fixed hysterical pain, criminal intents fleeted through our minds, or escapes such as truancy or sprees. We have not carried our fancies into execution because we have been endowed with the common sense which comes from security of school and home.

Family Background and Previous Personality

A great number of schizophrenics have no such secure roots. G. W. B. James is credited with the aphorism, "For every schizophrenic patient there is one schizophrenic parent." Genetic studies support him, and show how often the home environment is filled with woolly-minded, undependable, if not overtly unstable,

persons. (This is not an argument for environment as against heredity.) When such an individual is facing the adjustments of the post-pubertal years he does so ill-equipped, for the family offers no support or the accent is all wrong. The tendencies we normal persons believe we conquer defeat the patient.

But people are endowed with bodily characteristics as well as with mental attributes. Thus the body-build is often as tell-tale as the pre-psychotic personality (the thin test-tube type of physique, with cold extremities).

We attach the name of "schizoid personality" to the man who is without emotional warmth, incapable of genuine friendship, either coldly calculating or apathetically ineffective, a man who may never make a mistake but whom we would never trust. He hides within his carapace. Such persons often, though by no means always, constitute those from whom the schizophrenics spring. Other such personalities remain cold, detached, and only narrowly effective without ever developing the psychosis.

Early Symptoms

The youthful turbulence we have described in normal adolescents arises as much from unsteadiness in aim and thought as from rapid emotional changes. These thoughts and feelings are the reason why he seeks salvation for himself and his elders in excessive athleticism, fervent political loyalties, emotional religion, or becomes over immersed in reading and study. The inadequate frequently seek a haven in the Merchant Navy, which later they leave as impulsively. These passionate enthusiasms usually become integrated in a normal way because the youth feels he belongs to a society or to a new home, and such immature attachments are outgrown. With the schizophrenic salvation from health and beauty, the red-blue party, esoteric religion, or mystical cult are activities in which his thoughts but not his feelings find outlets. It is in this way that the early signs of the disease emerge. First the genetic background and environment play their part, and then we become aware of the attempts which are being made by the patient to control thought and feeling, or we are suddenly (though less often) faced with a florid psychotic disorder.

It cannot be too strongly emphasized that before the diagnosis is made we should be clear that we appreciate the patient's background. Hence, it is wise to be wary in diagnosing the disease in a person coming from a different social culture. Even some temperate Irishmen show conduct normal for themselves which would be psychotic if demonstrated by an executive officer of the Civil Service. A dock labourer's lack of finesse and feeling may be normal, but such signs appearing in an authoress would create surprise.

The morbid thoughts and speculations express themselves first through a falling off in normal interests, and the patient tries to concentrate upon examinations or factory work, and fails. He is described as being aloof and dreamy, and his appearance bears this out. He may explain spontaneously that things look and seem different. He may admit that he feels changed and that this change affects his head or his viscera. If asked to describe how he can explain it, the schizophrenic will either be unable to, or blame others or agencies rather than himself. Derealization and depersonalization, attributed to the operation of an outside power, are described in curious, quaint ways. One mark of the schizophrenic is that whereas with so many other patients we can sympathize and place ourselves in their position, or exclaim "There, but for the grace of God, go I," the schizophrenic's experience eludes us; we can almost get there, but never quite. Shakespeare has described these changes in an advanced condition:

> ". . . her speech is nothing.
> Yet the unshaped use of it doth move
> The hearers to collection; they aim at it,
> And botch the words up fit to their own thoughts,
> Which, as her winks and nods and gestures yield them,
> Indeed would make one think there might be thought,
> Though nothing sure, yet much unhappily."

It is this near-to-normal quality, yet not quite normal, which is the hallmark of early schizophrenic thinking. So, too, is the patient's conduct. There is a degree of inappropriateness rather than impropriety: turning away when we should expect enthusiasm; hilarity in place of quiet sympathy; over-activity where contemplation would better suit. When it is seen, the disdain and hauteur of the patient so unlike his previous self is pathognomonic.

Similarly convincing is a patient's complaint that his thoughts have been interfered with: they have been introduced into his head or body; they have been stolen—again from the activity of outside agencies. One caveat is needed. If these questions are asked directly *the answer should "click."* Mere passive acquiescence to the question may lead us astray. Near-defective, inadequate, or other patients may appear to suffer in these ways when they are merely obligingly answering affirmatively.

There are four objective signs of this interference with ideation. "Thought blockage" is the failure of the patient to continue a conversation. Instead it is punctuated by pauses in which he appears abstracted, thinking of things irrelevant. Sometimes the only sign of the disorder is that he will not answer our questions directly, a characteristic he shares with many defectives but capable of creating irrational antagonism in us. Mapother described the "knight's move" in the patient's associations, well illustrated by what the gentleman reported of Ophelia. Lastly, there is perplexity. Many early cases appear objectively only perplexed and we cannot tell why. There are plenty of perplexed adolescents whose difficulties we can appreciate. It is this unapproachability to the patient which is so striking. This difficulty shows itself early in those who promise they are going to do something and yet never do. The procrastinator admits his fault, is slightly ashamed, and does something. The schizophrenic smiles when taxed, gives an unconvincing promise, and does nothing. He finds it difficult to go to bed, or equally stays abed in the mornings though being wide awake for hours previously. He is said to spend his time idling, looking at a magazine yet not reading. A history of much time spent looking out of the window or into mirrors is suggestive. The loss of interest goes beyond apathy towards friends and current events. There is a loss of interest in those features of appearance which connect us with others; the hair on head and face is unkempt, the clothes are untidy, shoes are unbrushed, and nails uncut. Loss of libido comes early. Amenorrhoea may be present—transitory or permanent. Hypochondriacal concern, with curious speculative colouring, may be marked as a sign, though lacking as a symptom.

Differential Diagnosis

We have purposely only touched on the delusions, hallucinations, excitements, incongruous conduct, and stupor which mark the advanced disease, or the acute schizophreniform reactions. What is more difficult is to indicate the differential diagnosis. This includes prolonged and turbulent adolescence, hypochondriacal anxiety, obsessional states, criminal tendencies, slowly developing intracranial disease, and, most important of all, hysteria and depressions.

If we bear in mind how often schizophrenia is a gradual process, and how the cardinal symptom is disordered thought, we shall realize that the mind has time to marshal all its resources against the mental undermining which these strange thoughts imply. It may well be found that modern empirical treatments are effective because they help the mind's defences. All the different mental syndromes we have just enumerated may be essential accompaniments of the disease, representing the results of an attempt to limit it.

The distinction from an unusually turbulent adolescence, with impulsive and thoughtless acts, wild accusations, scenes, and psychopathic behaviour, rests upon the maintenance of affective sympathy. If we accept the youth's premises (false though they be) might we have done the same? With the neurotic we should answer, "Yes." With the schizophrenic we should answer, "No"; with him one premise at least or its resultant act is inexplicable and more often strange if not "clear balmy."

Hypochondriacal anxiety is very common in the teens and twenties. In the non-psychotic it emerges as a sign or warning of emotional conflict, and, though it may have features of strangeness in the neurotic, these can be explained by lay ignorance or superstition.

Obsessional neurosis is a most thorny problem, especially since the more bizarre compulsions lead on to the psychosis. As Stengel has pointed out, the obsessional ruminations, philosophizing, writing, or rituals may be defensive against the disease. What we find in the non-psychotic is obsessional anxiety with marked insight into the symptom's abnormality—"It is absurd to have to check this, but I simply must"—or the persistence of an original fear which is used to justify an unwillingness to travel, for example, or to alter a course. Frequently the obsessions have been present with long intermissions. The obsessional concerns of the early schizophrenic are more speculative than anxiety-producing. They justify rumination, but this is odd, detached, without meaning to us, but with much personal meaning to the sufferer. Again we are aware of the safety-curtain between us and the stage upon which the schizophrenic drama is being enacted.

Two widely held misconceptions must be dismissed. The first is that the affect is incongruous, shallow, or absent. At the beginning it may be wholly appropriate to the odd beliefs, a little later depression is wholly reasonable, and suicide not uncommon, often executed with a macabre flavour which is the sign-manual of schizophrenia (e.g., disasters at public schools).

The second must be to deny the erroneous belief that hysterical manifestations do not accompany schizophrenia. The anxiety generated by the self-observed changes may be apparently dismissed by the sixteen-year-old schoolgirl, yet thought disorder is so disturbing that it may result in conversion symptoms and produce apparently "hysterical" physical sensations. Such symptoms tend to be less clamant than in the hysteroid personality. Anything odd about the flavour of a hysterical complaint in an adolescent who has recently lost interest, lies abed, and is becoming dreamy, must not be dismissed.

Two rare manifestations merit mention: fugues may initiate the illness; and, in my opinion, self-mutilators are schizophrenics. There are many anxious, hysterical, obsessional persons whose symptoms arise because they are fighting for months or years their secret detachment and misunderstanding of others, which not only perplex them, but which they know at the beginning have a bizarre flavour cutting them off from human sympathy. It is our privilege to be approached and receive their anxious secrets and act as if we believe *puto nihil alienum humani est.*

Cerebral abscess and intracranial neoplasm may commence with thought disorder and go on to abnormalities of conduct. Careful neurological examinations must be made. Psychopathic personalities and defectives when in difficulties may behave in strange and unpredictable fashion. Here one must emphasize that an adequate history is essential, not of the illness alone, but of the person's past achievements and clinical history. It is here that we need to envisage something of his cultural background.

After one has canvassed all the possibilities presented by the patient, one is often left with little certitude except that the relatives will be loath to co-operate in accepting hospital treatment. Schizophrenia, despite all its implications, is a disorder which should be met by ordered hope, great patience, and readiness to press for observation of the sufferer in suitable surroundings. Now there are not only hopeful methods of treatment, there are diagnostic aids with investigation by barbiturate injections and tests such as the Rorschach which can clarify this difficult field.

One final word: severe temporary stress (such as military conditions) and frustration may produce extremely paranoid conduct, impulsiveness, ill-matched aims. In our present post-war society these reactions in the harassed partners of a marriage seem commoner than they were. They may certainly proceed to an irreversible schizophrenia or an irreversible frigidity. Considerable expenditure of time and energy spent in elucidating such cases may not pay a large dividend yet a worthwhile one.

Correction.—We much regret that owing to a printer's error the dose of phenobarbitone was wrongly given as 1 g. instead of 1 gr. in the second paragraph under the cross-heading of "Treatment" at p. 1443 of Brigadier Boyd's article on "The Dysenteries."

Nurses and nursing auxiliaries engaged in periods of training or taking refresher courses in the National Hospital Service Reserve will not, while so engaged, be liable to pay national insurance contributions as *employed persons* except when they render services in the reserve for 24 hours or more in any contribution week (National Insurance (Classification) Amendment Regulations, 1951). The nurse or auxiliary who does less than 24 hours' service in the week will in general (if she has no other employment in that week for which an employed person's contribution is payable) remain liable to pay a contribution in Class 3 or, if ordinarily a self-employed person, in Class 2. The regulations do not affect the liability for payment of industrial injuries contributions. These contributions are payable no matter how short the period of employment.

METHODS IN MEDICAL TEACHING

CONFERENCE-COURSE OF POSTGRADUATE MEDICAL SCHOOL

The Postgraduate Medical School of London arranged on June 22 and 23 a conference-course on methods in medical (mainly undergraduate) teaching. Over 400 accepted invitations for the course, which was held at the London School of Hygiene and Tropical Medicine. Dr. C. E. Newman, Dean of the Postgraduate School, presided at the first session, and subsequent chairmen were Professor Ernest Finch, Professor J. McMichael, and Professor Ian Aird. An extraordinary amount of interest was taken in the event, and the course could have continued for another day or longer.

Aims of the Medical Teacher

Sir FRANCIS FRASER, in an opening address, declared that all medical teaching must be at university level. It had been suggested that, while the preclinical years were properly the responsibility of the university, the clinical years, devoted as they were to instruction in practical methods and acquisition of skills, might be spent in institutions not necessarily of university standard in equipment and staff. But medicine was not technology. It was the university which endowed a man with capacity for discrimination, with breadth and vision. The university was a community of teachers and students, and the contact of the groups gave the student a knowledge of humanity and a trained intelligence.

In the clinical years there was no danger of the applications of knowledge being neglected; the danger was rather that they should become dominant and over-exciting. Medicine was both an art and an applied science, but it was rare to find a situation in which the evidence was sufficiently complete to justify a conclusion on scientific grounds alone, and the medical practitioner had constantly to fall back upon experience. Nevertheless, the teacher must look for every opportunity to apply exact science, developing in his students such habits as history-taking and physical examination so as to have knowledge of all the facts available. The patient must be regarded from the physical, psychological, and social points of view, and concerning the social aspect he suggested that most medical teachers knew very little about the services provided by local authorities. Sir Francis Fraser concluded by saying that the most fruitful method of medical teaching had been left out of the programme of the course—namely, the influence of the personal example of the teacher.

Dr. R. D. LAWRENCE said that, stimulated by its Educational Number, he wrote a letter to the *British Medical Journal* two years ago in which he asked who was going to teach the teachers. He pointed out that capacity for teaching was practically never taken into consideration when an appointment was made to the staff of a teaching hospital. As a result the Royal College of Physicians set up a committee on the teaching of teachers. Dr. Lawrence mentioned diction and delivery, and quoted from the *Lancet*: "Many medical teachers are inaudible; they bury their noses in their notes, and address their boots, the blackboard, the ceiling, anything except their audience." At least at the registrar stage some critical process should be applied to diction and delivery in medical teaching. What was the good of talking to students if they could not hear? Students might much more profitably be in the library reading the textbook one had not written.

In all discussions on medical teaching it was agreed that too much detail was taught, there was far too much memorization. What should be taught were general principles. But how could the general principles of diagnosis be taught? The mental processes of the expert clinician were such that, by the time he looked at his patient and heard his first few words, he had made a provisional diagnosis, and from then onwards he was going backwards and forwards in a very subtle and difficult way. How could this be taught to the student?

The Teaching of Diagnosis

Dr. RICHARD ASHER agreed with Dr. Lawrence on the difficulty of teaching diagnosis. The more efficient a clinician was in the making of a diagnosis the less certain was he of his reasons for making it. He likened diagnosis to the instinctive way in which one pushed or pulled a door; one did not pause in front of a door and work out the mechanics of the operation. Indeed, if the diagnostician did think about his diagnosis he would be like the centipede who was asked which leg came after which—

> "Which wrought his mind to such a pitch,
> He lay distracted in the ditch,
> Considering how to run."

Yet the teacher who had to tell his class, "I cannot say why, but I somehow feel this man has typhoid," was not a good teacher, though this might impress his students.

Dr. Asher also suggested that students should be taught to be critical of literature. There was a tendency for students to read the latest articles and be greatly impressed by them. They read the medical journals before they should.

Dr. C. E. NEWMAN said that diagnosis, like all other real skills, was essentially unconscious, and teachers had to acquire the incredibly difficult art of analysing an unconscious process and explaining "how they did something which they did not know how they did." He also raised the question of the object of medical education: whether it was to produce a good general practitioner. He suggested that it was to train an undifferentiated good doctor, and another speaker said that what they should try to turn out was simply a graduate—a potentially good doctor, who could turn to medicine or to surgery as a specialty.

The Formal Lecture

Professor IAN AIRD had some pawky things to say about the formal lecture. A lecture had been defined as a convenient mechanism for the passage of facts from the mouth of the lecturer to the notebooks of the students, without passing through the mind of either. The lecture was the Cinderella of teaching. In university common-rooms it was said that a man would apologize for or even conceal his ability as a lecturer, lest he be dubbed meretricious or a charlatan. The lecture must still remain in most universities because of its cheapness, but though cheap it need not be nasty. Hippocrates was known to have been an effective, perhaps eloquent, lecturer. Fallopius, Eustachius, Linacre, John Hunter, Paget, and many others lectured with profit. The aim of the lecture was not to extract the essence of the library, but to bring sunlight through the library windows, to take the smouldering coke of students' minds and by some alchemy of personality transform it into incandescence.

A bad lecturer was not only a slur on his university and an embarrassment to himself but a waster of students' time. The lecturer should have a wide knowledge of his specialty and experience in its practice, should have made some original contribution to his subject, and should be able to teach. At the same time the born lecturer was open to some dangers—he was liable to over-teach, to dramatize, to sacrifice truth for aphorisms. At the other extreme was the introvert who found lecturing difficult and did it badly—the kind of lecturer whose head was bent over his notes, and who, when a student in the front row asked, "What was that, sir?" looked up and said, "I am sorry, I did not know I was overheard."

Note-taking, said Professor Aird, was a primitive occupation, for notes could be taken more accurately and comfortably from textbooks. Yet note-taking, properly done, was an excellent intellectual exercise, and might be profitable for more junior students. The teacher should interest himself in his students' notes, although too elaborate notes made the university teacher a kind of coach, and coaching was the unimaginative presentation of facts.

He then went on to certain details of lecturing. The lecturer should be careful about his dress, which should

be neat but not gaudy, with nothing—certainly not a startling tie or a monocle—to distract attention. One speaker the following day, by the way, mentioned that a lecturer should not come to the lecture desk in his overcoat. The lecturer should fix his gaze on the man in the middle of the second row from the back. He could use his eye for discipline, not staring out the unruly student, but focusing on a point a little above the bridge of his nose, which was very confounding. As for the voice, not all of them were equipped with the necessary accessory sinuses for a booming voice, nor was that required. Every lecture-theatre should be fitted for amplification. Speed of delivery should be neither too fast nor too slow. Pauses were important. The lecturer should, if possible, listen to himself on the dictaphone—a humbling experience. He must eschew distracting habits, such as walking from side to side of the lecture table. One famous lecturer was accustomed to walk up one gangway and down the other, his class watching him as if they were watching slow-motion tennis. It was well to have a striking opening. One eminent cancer specialist who came to Hammersmith began: "Cancer! Gentlemen, do you fish? Why does a trout stop growing?"

Clichés should be avoided. It would be a good discipline never to use the word "case." There should not be too much humour, and what there was should be good-natured. In short, the lecturer should know himself, know his subject, and know his students. In some discussion following Professor Aird's lecture, notes taken at lectures were criticized as useless; and the same was said of lantern slides. One contributor held that there should not be more than one lecture a day, preferably given just before lunch. The proper duration was regarded as 45–50 minutes. It was also considered that indecisive or incomplete research should be kept out of lecture teaching.

The Lecture-demonstration

Sir STANFORD CADE carried out a lecture-demonstration with two patients. The object of a lecture-demonstration, he said, was to convey something that no books or formal lectures could convey—namely, living medicine or surgery. It was teaching by example; it appealed to the intelligence, not the memory, and it aroused the critical faculty. If he was asked who was the ideal lecture-demonstrator, he would answer, "Ruth Draper." If he could catch the students' imagination as she caught the imagination of her audiences he could carry out a lecture-demonstration even in the absence of the patient.

The first of Sir Stanford Cade's two patients was a woman who had had pulmonary tuberculosis, for which a thoracoplasty was performed ten years ago, and who, seven years ago, developed a tumour of the breast, for which radical mastectomy was done. Later she developed nodules in the other breast, and the same surgeon, whose views had altered in the meantime, now performed simple mastectomy. There was excellent healing on the side on which the radical operation had been performed, but, on the other, telangiectasis had developed and the arm movement was less free. The other patient had a rodent ulcer on the forehead. This was of an extensive character, but, having been painless, he had sought no medical advice for several years. Sir Stanford Cade demonstrated these cases as if he were talking to students.

Dr. F. M. R. WALSHE followed with a similar lecture-demonstration on a patient with progressive paraplegia, which had shown its first sign in loss of temperature sense. He affirmed that he had no philosophy concerning the lecture-demonstration, and no technique. The difference between the formal lecture and the lecture-demonstration was the difference between the general and the particular. The formal lecture, like the textbook, was made up of generalizations, but in the practice of medicine it was particularization that the doctor needed, and the lecture-demonstration seemed to be the only way in which the art of dealing with the particular could be conveyed.

In discussion it was suggested that many conditions—early cardiac disease, for example—were not suitable for lecture-demonstration. One speaker thought that if discussion took place in the presence of the patient it was likely to be embarrassing, and if the patient was removed before discussion he was likely to think that something was being concealed from him; also that the word "tumour" should not be used before the patient. Sir Stanford Cade, however, said that patients were comforted by the word "tumour." "It is only a tumour; I was afraid I had got cancer." The ideal number in attendance at a lecture-demonstration would be between five and ten.

Bedside Instruction

Professor G. W. PICKERING spoke briefly on the technique of bedside instruction. He said that there was probably no form of clinical teaching in which it was more profitable to teach method than at the bedside. By "method" he did not mean simply technique, but the manner of collecting, checking, and interpreting facts about the patient. Bedside teaching was intimately related to clerking and dressing. The teacher should consider clerking and dressing from the student's point of view. There was nothing more discouraging to the student than to feel that his notes were not going to be read and would be passed to the waste-paper basket.

The student wanted several things from his teacher. In the first place, he wanted his work appraised, he wanted to know whether he had done it well or badly, and how it could be bettered. Secondly, he wanted some help in interpreting the facts he had collected. He wanted to know what was going on in the patient in terms of disturbed structure and function, and how to identify the type of disease process which had led to these disturbances, and why it should have arisen in that particular patient. The student wanted to feel himself a responsible member of the team, and that the patient was helped to some extent by the work he was doing there.

In outlining a typical session of bedside instruction, Professor Pickering said that the optimum number of students was one to six, and should never exceed ten. The audience should sit; the brain was more receptive when the body was at rest. The optimum duration was about an hour, the maximum ninety minutes. He also emphasized the necessity for the teacher to be kind to the patient—bad manners were always out of place—and to be kind to the students, not endeavouring to score off them. Asked about students' notes he said that they varied very greatly in value; some were worthless, but others as valuable as any they had. In his hospital they always kept the students' records.

Clinico-physiological Discussions

Professor ROBERT PLATT said that during the last two or three years at Manchester Royal Infirmary they had developed clinico-pathological discussions for students who were doing physiology and had never been in hospital before. There was no attempt to teach them the technique of examining cases; that was learned later when they came to the introductory clinical course. The discussions were started during the students' third term in physiology, when they had already "done" the cardiovascular and respiratory systems and were learning about the blood. They came in groups of about 30 at a time, and the professor of physiology and usually one lecturer came with them, and he (the professor of medicine) took the chair. He and his staff got together and tried to reconstruct exactly what happened at the last examination. He started with a few remarks about the objects of the discussions on applied physiology, that they were to give an insight into what the students were learning at present and what they would go on to learn in the wards. The patient was then brought in and introduced by one of the doctors; the history was taken and the simple physiological appearances were demonstrated. Then another of the doctors would take up the story, after which the patient, duly thanked, would go out. Professor Platt then gave an outline of the discussions and exchanges which followed.

The subjects covered, with different groups of students, were anaemia, congestive heart failure, cyanotic pulmonary

disease, acute haemorrhage, diabetes, renal oedema and failure, steatorrhoea, thyroid and parathyroid disease, and upper and lower motor neurone lesions. The proceedings at a discussion took as long as 1½ hours, and there was no flagging of interest. It was difficult to get students' questions, and a good deal of the discussion was sustained by the staff. There were only a limited number of topics which lent themselves to this form of treatment, but he felt that this was one of the most successful things that they had done in medical teaching. The students were given the feeling that they were doing something real, that they were on the way to becoming doctors, and it was of benefit to the joint medical and physiological teaching staff.

In discussion it was suggested that the same technique could be applied occasionally with reference to anatomy as well as physiology. Peripheral nerve injuries could be helpfully demonstrated. Dr. JAMES LIVINGSTONE suggested that the haematologist and the biochemist might occasionally be invited to the bedside and make their contributions. It was remarked that students' questions were generally on the human side—about treatment and prognosis—rather than on the scientific.

The Young Teacher

On the second day of the course Professor M. ARNOTT opened with the contribution of the younger teacher to medical education. Age and development in teaching capacity were not necessarily correlated. There were elderly Peter Pans and, conversely, old heads on young shoulders. But older teachers like himself, looking back on their early days, were rather appalled at the recollection of their glibness, their assurance, the absence of the voice which now whispered in their ear, "You must not say it that way. You must not attach that emphasis to it. You know, that is not really sound." The teacher should not over-simplify or talk down to the dullest in the class; medicine was no field for the dullard, nor even for the average person.

It was important that those beginning to teach should be engaged in scientific research, clinical or otherwise. They all knew the kind of person who liked teaching, but not research. When he encountered an individual with such views he did his best to prevent him from getting an opportunity of perverting the mind of the young. Such a teacher would be popular with students; he would talk all the time, asking questions which he would answer himself to his complete satisfaction, but he would not change from year to year and would do nothing to advance knowledge. Teaching, after all, was not the handing on of the same body of knowledge from one generation to the next; that would stultify evolution. "University teaching is the teaching of what is not known rather than of what is known." The young teacher should be encouraged to develop happy relations with the students. He should be cautioned against going on for a long spell without bringing the students into discussion. The teacher who acquired a complete set of notes on any subject was lost. The sooner he could do without notes altogether the better teacher he would be.

Professor IAN AIRD said that as a student he was very grateful to his immediate seniors under whom he served his initial clinical apprenticeship. It was from house-physicians and -surgeons that the student got a great deal of instruction in such matters as catheterization, anaesthesia, tapping of chests, and performance of lumbar puncture. There was no gap between the first year of the house-surgeon and the final year of the student.

In some further discussion on this subject the view was put forward that there was no antagonism between research ability and teaching ability. Research was an important safeguard against too much didacticism in the teacher. One speaker said that a main difficulty which the student encountered was the mass of people who were not able to teach and never would be. Were there no means by which people incapable of teaching could be released from this duty for the rest of their lives? There ought to be some method whereby students could let them know whether they were being taught effectively. Other advice given to young teachers was to classify their ideas and the presentation of them, not to be afraid of using eponyms, to emphasize the more important points by repetition, and to bear in mind that listeners tended to fall asleep.

Technical Clinical Methods

The subject of technical clinical methods was briefly introduced by Mr. JULIAN TAYLOR, who addressed himself to the question of taking a young man and turning him into the beginnings of a surgeon. When people saw an experienced surgeon operating they were apt to say how easy it was. It was an example of the art which concealed art. He stressed in particular the importance of teaching the young surgeon to be gentle.

Professor ERNEST FINCH said that, sitting on committees as an assessor, it was distressing to him to find men who were seeking posts regarding themselves purely as surgical technicians. They would claim proudly that they had done 80 gastrectomies—that appeared to be the great yardstick of a surgeon's ability. Many of these men were ready to take posts in busy industrial places, where they would be called upon to deal with fractures and other injuries, but their interest seemed to be in the alimentary canal. He deplored the tendency to produce a breed of technicians—slick operators. It would be the worst thing that could happen to British surgery. These men did not know *when*, but they knew how; and that got one nowhere. He hoped that some form of postgraduate teaching would correct the tendency.

Sir JAMES PATERSON ROSS said that one of the most regrettable changes in practical medical education during the last 30 years was the disappearance of any sense of responsibility from the student; it was transferred to those who were more senior. In his own hospital it had become a rule that no student should ever send a patient away, no matter how trivial the condition from which he was suffering. It might be said that that was a sound rule, but in days gone by they learned a great deal from having a sense of responsibility. The present tendency had led to students not even doing dressings in the wards.

Teaching in the Out-patient Department

Mr. A. J. GARDHAM spoke on the technique of teaching in the out-patient department. One of the great advantages of that department for teaching was that there the teacher's mind was continually at work on a fresh problem. This did not happen in the wards or in lecture-demonstrations. When the teacher was working on a fresh problem he must go slowly and resist the temptation to short cuts. He himself insisted on having everything written down by his dresser in longhand. The teacher, in his first contact with cases in the out-patient department, might make mistakes, and it was important not to attempt to conceal them from the student, who was probably aware of them anyway, but to use them profitably, going back on himself and doing it again. The close relation to the patient which obtained in the out-patient department never happened again to the same extent, for once the patient went into hospital he was to some extent regimented. It was worth remembering that it was in the out-patient department that the student saw the vast preponderance of suffering humanity who were not textbook pictures. At all events, the textbook pictures did not turn up in his own department.

Again, it was in the out-patient department that immediate decisions had to be taken, whether the condition should be treated or left alone, and one of the points of usefulness of the department in teaching concerned not only the cases which were treated but the cases which were sent away. Owing, again, to the closeness of the relation with the patient, one could in the out-patient department cover a very large number of the little gaps which were left open in ward teaching. The department was not a bad place also to start the student learning how to behave to patients. A broad hint could be given if a not-too-clean hand were

placed on the abdomen, or a laugh were heard at the wrong moment, or a careless word which might afterwards worry the patient were uttered.

Mr. Gardham thought that detailed pathology should not be taught in the out-patient department, but one should stick to very simple issues. He tried not to mention rarities and to keep everything on the ground floor, also to avoid talking about niceties of treatment. The student who got his physical signs right nearly always gave a good account of himself in other directions. As to the arrangement of out-patient sessions for teaching, he mentioned, only to condemn, the practice at one hospital where the surgeon, at a first session, took the physical signs, and at a second session the same week had back again the best cases on which to teach. The logical conclusion of such a method would be to have a panel of whole-time patients. There was probably no best solution. His own method was to plough through the cases as they came, not collect them, and try to show the students the way in which his mind was working. If he came across a case with good physical signs he went over them with his registrar, and afterwards left him behind with some part of his audience to demonstrate them.

Out-patient Teaching of Paediatrics

Sir JAMES SPENCE expressed his strong disapproval of the old German clinical lecture, which he thought a thoroughly bad instrument of teaching. His experience at the Johns Hopkins 20 years ago had also chilled him towards the clinico-pathological conference. What he had to say about out-patient teaching applied more to paediatrics than to any other branch of medicine. It offered a situation in which one had the presence of the mother who had observed the symptoms in her child, and the paediatrician had to combine the roles of judge and examining counsel. This brought out factors in the technique of examination such as practically no other branch of medicine could elicit. He regretted the divorce between general medicine and paediatrics—though he was not afraid of its effect on paediatrics.

Points to bear in mind were that very often in such consultations the parents would not confess their fears and doubts in the presence of a third party; the student must be told that he would not be allowed to examine the patient, but he would see the teacher tendering explanations and advice to the person who had sought his opinion. There were three diagnoses to be made in paediatrics. The first was as to the presence or absence of the organic disease which the symptoms suggested. The second was as to the concept of symptoms or the fear which the mother entertained. The third was as to her ability to understand and follow the advice given.

On the question of design of the out-patient department, Sir James Spence suggested that a house should be taken for the purpose. The house should have small rooms, with only two students to a room, and it should be called the out-patients' consultation centre. In speaking, as Mr. Gardham had done, on the teaching of behaviour to the students, he said that he had received a letter from America, from someone who had been attending his own department in Newcastle, saying how impressed he had been with the courtesy shown to patients by the students, as, for example, in getting up and opening the door for them when they left the room. Professor ROBERT PLATT urged that, in dealing with out-patients, the patients should not be seen and selected beforehand by somebody else.

Pictorial Teaching

Dr. P. N. CARDEW gave a demonstration of pictorial teaching. It was important not to overlook this factor, because the majority of people, including students, tended to think in visual terms. He spoke mostly about lantern-slides, the most commonly used—and abused—of all the methods at their disposal. A frequent fault with diagrammatic slides was to overcrowd them with information which could not be absorbed during the minute or two they were on the screen. He showed one such slide from which six slides could easily have been made. Slides should be viewed not more closely than two or three screen-widths away, and not further than six screen-widths—a condition difficult to fulfil in a lecture theatre—and the angle should not be greater than 60 degrees. Lecture theatres might well be designed diagonally to assist screen viewing. He gave some advice on the proper size of legend on lantern-slides. A useful rule was that, as letters in ordinary typescript were 2 mm. high, 6 in. (15 cm.) was the largest amount of typescript that should be covered in a slide. The total area of typescript on a slide should not be greater than was contained on a postcard. He preferred white lettering on a black ground to the reverse. He considered the filmstrip of small advantage in teaching, and, as for films, their only justification for teaching purposes was when they showed (as in ophthalmic operations) more than could be seen with the naked eye or (as in exercises of recovering paralytics) dealt with subjects which themselves had movement.

Professor IAN AIRD said it seemed to him perfectly clear that even though a professional photographer was employed at a teaching hospital it was a great advantage to have the services of a medical consultant on the use of illustration as a teaching instrument.

Young Graduates and Research

The last subject of the course, the introduction of young graduates to research, was brought forward by Professor H. J. SEDDON. He said it was very important when people came along with some proposition for research that they should be asked to search their hearts. A variety of motives actuated people to say they wanted to do research. They might be in a place where research was a fashionable thing to do, or they might have an eye on a higher appointment. One was thankful that the business of writing papers was not regarded as a necessary preparation for preferment in this country.

Research was largely a matter of the spirit. The whole idea of research had been dramatized in fiction, and when an account of a discovery was published it read marvellously. But, of course, the work did not start or go on in that way. It was for the most part an undramatic form of activity, and it required spiritual endurance of a high order to carry through. It was said of great musicians that their success was due, 10% to ability, 10% to good fortune, and 80% to hard work. The same was true of the research worker. Moreover, he had to achieve a kind of mental dichotomy. He had his responsibility to his patients, which was paramount, and at the same time he was using his patients and the phenomena they presented as a means to an end. By the way, he must never go so far in that respect as to refer to his patient as a "preparation."

One of the powers that must be cultivated was concentration, and with it went the ability to say "No." Not too much of his time must be allowed to go into routine work; also (a heavy price to pay) he must forgo being an all-round man at his job as a clinician, and again, at times when there was a great detail of work to be done, he must forgo social pursuits. Clinical research must obviously be carried out within the busy walls of a hospital, so that he must be a guardian of his own mind and produce for himself the atmosphere in which he could work.

What could be tackled in ordinary clinical research? First, the natural history of disease. Such a thing, for example, as knock-knee, formerly supposed to be due to rickets, but persisting after the abolition of rickets. Secondly, the results of treatment. An investigation going on at the present time concerned the effect of streptomycin in joint tuberculosis. Thirdly, the investigation of some complaint or phenomenon with the object of finding out just what it amounted to and what was its cause.

The Qualifications of the Research Worker

Professor J. MCMICHAEL said that all clinicians in a sense were doing research. If, in a university department, they concentrated on more esoteric techniques, this was only

because they were equipped to do such work. Research was really an extension of clinical experience. Factual teaching in the wards left many unanswered questions, and these were the questions to which they addressed themselves. Each research unit should give facilities only for the kind of work for which it was equipped. One line of work should be enough for one director or head of a group. They should be able, certainly within a year, perhaps within six months, to say whether someone who had offered himself as a research worker had the necessary flair or qualities of character to be continued in that employment. The worker should be familiar with the most recent articles on his subject, but the important thing was that he should get down to laboratory work and develop a sense of technique, and it was when that was done that he could read the literature to the greatest advantage.

Professor McMichael stressed the necessity for careful documentation, the avoidance of the too early formation of hypotheses, and the desirability of bringing in at the appropriate point someone who was statistically minded. Research which was merely of the form-filling type should not be encouraged. The research worker must do things with his own hands. He must be responsible for the accuracy of laboratory determinations and observations. In writing his paper it might be necessary to draft it half a dozen times before attaining a presentable script, and here the speaker paid a tribute to the editors of the medical scientific journals for the way in which they edited the many ill-constructed scripts submitted to them. Finally, the research worker must never forget that he was a trained clinician; otherwise there was a danger that a separate breed of clinical pathologists would arise.

Reports of Societies

FESTIVAL SYMPOSIUM ON BURNS

Under the chairmanship of Dr. LEONARD COLEBROOK, F.R.S., a symposium on "Burns" was held at 1, Wimpole Street, London, W.1, on June 19. This was the 12th of the Festival Scientific meetings arranged jointly by the British Medical Association and the Royal Society of Medicine. The first four papers were presented by members of the staff of the Medical Research Council's Burns Unit, at the Birmingham Accident Hospital. The fifth paper, on the use of homografts for extensive burns, by Mr. Rainsford Mowlem, was preceded by a tribute to Dr. Leonard Colebrook for his work on infection and its control, most of which had been accomplished through his own enthusiasm, backed by the establishment of the M.R.C. Burns Unit. Finally, Mr. A. B. Wallace, of Edinburgh, recapitulated briefly the details of the exposure method of treating burns and its technical difficulties.

Fluid Replacement

Dr. J. P. BULL described the various physiological problems which burns produce. There was increased permeability of the capillary bed from which large as well as small molecules escaped, the lymph oozing out having much the same protein content as plasma. The total plasma loss was not immediate and continued for twenty-four hours or more, and the fact that the patient did not appear shocked in the early stage was no justification for withholding treatment if the area burnt was sufficiently large.

The body's attempted method of correction was by vascular constriction and redistribution of extracellular body fluid. For small burns this, together with the administration of oral fluids, was sufficient, but the electrolytes lost should be replaced by adding some sodium salts to the drinks. A solution of 0.4% sodium lactate with glucose and fruit juice was recommended. Burns in adults involving 15% of the body area and in children 10% of the body area required intravenous therapy. A simple method of calculating the area involved was to allow 9% for the head and neck, 9% for each upper limb, 18% for each lower limb, and 36% for the trunk. The ideal replacement fluid was plasma and its administration was best controlled by observing the clinical state of the patient, repeated haematocrit estimations, and a watch on the urinary output, for which the use of an indwelling catheter was recommended. The quantities of plasma required were thus controlled by a running assessment of the patient's condition, though a rough approximation of the fluid required could be made by allowing one to one and a half litres of plasma for each 10% of burn area. Half of the quantity of plasma required should be given in the first six hours and the remainder over the next eighteen hours. A further small volume might be needed after this. While there was some red cell loss this was not important in the early stages, and the administration of blood immediately after the burn interfered with the interpretation of the haematocrit readings. It was more convenient to give blood at the end of the shock phase.

In view of possible difficulty in obtaining sufficient plasma, a search had been made for plasma substitutes. These must contain molecules similar in size to plasma protein, and of a number tried dextran, which was a carbohydrate whose molecular size could be varied easily, appeared satisfactory and could be administered in quantities equal at least to the body plasma volume with apparent efficiency and safety.

Control of Infection

The fresh burn was sterile, and Dr. E. J. L. LOWBURY described methods of control for preventing the development of infection. Clinicians were not only concerned with gross infection with toxic effects, but with silent infection with organisms such as *Streptococcus pyogenes* which might inhibit the taking of grafts and increase the tendency of scars to contract.

Control of infection could be divided into two parts: prevention of infection when the burn was being dressed, and the protection of the burn in the ward. A special dressing-room had been set apart for burns in which filtered, heated, and humidified air was blown at a constant rate to control airborne infection. Nose and throat swabs were taken from both the patient and staff, and dressings were carried out by "no-touch" technique. The wounds were dressed with penicillin cream, containing 1,000 units per gramme in a "lanette wax" base. Firm pressure and support were then applied to the skin area to prevent movement, by plaster-of-Paris if necessary. It was essential to change dressings which had become soaked in exudate. For difficult areas, such as the buttocks, and circumferential burns exposure treatment with the insufflation of penicillin powder was recommended. Nothing was more important in the prevention of infection than the early skin grafting, when possible, of full-thickness skin-loss burns. It had been shown that 67% of burns grafted on the day of admission remained uninfected, while only 16% grafted at a later date were clean. *Staphylococcus aureus* and *Pseudomonas pyocyanea* were the most difficult organisms to control. Polymyxin had proved useful for *Ps. pyocyanea* and coliform bacilli; grafts had taken more effectively when a mixture of polymyxin and penicillin was employed than when penicillin alone had been used. Aureomycin had been found of value in infection of *Staph. aureus*.

Physical Signs which Indicate the Need for Grafting

There was general agreement that full-thickness skin loss should be excised and grafted on the day of burning if the patient's condition and the size of the burn permitted this course. Mr. D. M. JACKSON then went on to describe the difficulties in assessing the area of total skin loss.

The appearances of a burn or scald in the early stages depended on the intensity of the burn and were not related to the depth of tissue destroyed. Burns could be divided

into three zones: the peripheral zone of hyperaemia, the intermediate zone of capillary stasis, which often thrombosed later, and the central zone of coagulation, usually white unless charred. Zones two and three subsequently sloughed off. It was only when these zones penetrated the full-thickness of the skin that total skin loss occurred. Early observation of the circulatory changes in the burned area was unreliable in deciding whether the skin was viable or not, but estimation of the sensitivity to pin-prick was a helpful guide in delimiting the area of partial skin loss. In dealing with burns of the face, palm, and sole the attitude should be conservative and excision of areas of doubtful vitality was contraindicated. On the other hand, healing on the back of the hand was notoriously poor and early excision was advisable. Some of the later appearances of burns were then described to show how these were related to the need for grafting.

Early Skin Grafting

Further technical details in the treatment of burns by primary excision were given by Mr. W. P. DALLAS ROSS. Excision and grafting should be carried out where possible within six hours of the injury. If the patient was seen later, twenty-four hours should elapse so that the burnt area could be cultured for pathogens. Burns of over 10% body area in children and over 15% in adults were too large for immediate grafting. Treatment of the shock precluded operation.

The majority of burns excised were usually small and mostly involved the hands and feet. All the totally destroyed skin must be removed including, in mixed burns, a small margin of the partially damaged skin. The depth of the excision rarely caused difficulty. Absolute haemostasis was essential; this was obtained by hot packs, elevation of the part, and spraying with a mixture of fibrinogen and thrombin. Excessive blood loss was made up at the time by transfusion. Usually repair was done with split-skin grafts, but for deep burns where bones and tendons were exposed a flap graft was necessary. Where grafts failed, regrafting should be done as soon as possible. In burns unsuitable for primary excision and grafting the operation was only delayed for the elimination of haemolytic streptococci. Postage-stamp grafts were not desirable and, where it was necessary to use them owing to a shortage of skin, they should never be placed more than ¼ in. (6.3 mm.) apart. Where there was much skin loss the stage planning of the operation might be complicated. It was better to graft a limited portion of the burn completely than to patch-graft a large area with wide gaps between the grafts. Preservation of the grafts in a refrigerator and their application without anaesthesia at a later date was often helpful.

Homografts for Extensive Burns

Mr. RAINSFORD MOWLEM paid tribute to the experimental work of Professor P. B. Medawar in the study of homografts in animals. It had been shown that these grafts normally lasted for about seven days, and were then shed. During this phase, however, the animal apparently acquired an intolerance to the transplantation of such tissue and subsequent grafts were discarded earlier. Medawar had shown that cortisone prolonged the life of the graft but reduced the formation of granulation tissue. A similar result had been obtained by radiation (B. Lennox), but the dosages used were impracticable for the human being.

In both the experimental and clinical fields much remained to be done. In man, homografts normally lasted from 15 to 25 days, and were sometimes of value in resurfacing extensive areas as a life-saving but temporary measure. The application of homografts and autografts side by side had, however, not been followed by lysis of the former. It seemed probable that they were replaced by ingrowth from the autografts. This process occurred without visible death of the homografts. The exact method of replacement was not clear, but invasion had been shown to occur (Stuart Gordon). Grafts from multiple donors were more successful than from a single donor, probably because they elicited less mass reaction. A curious pigment change which left the homograft a pale grey colour for many months was not yet understood.

Exposure Method of Treating Burns

In the short time left to him Mr. A. B. WALLACE could do little more than outline his method of treatment. The chief principles were the same as for the treatment of burns by other methods, but the additional important factor of drying the burnt area reduced infection very effectively. The burn was cleansed under aseptic conditions using cyclopropane anaesthesia. Blisters were snipped and washed with hypotonic saline, and the area was then dusted with lactose containing 10,000 units of penicillin per gramme. The powder was insufflated every four hours. The treatment was particularly suitable for burns of the face and one aspect of the trunk (allowed up on the fourth day), and burns of the genitalia. More difficult areas included the neck, where the effective formation of crust was slightly delayed by movements and skin folds, and the hands and fingers, where support to allow adequate treatment was difficult but not insuperable. Satisfactory results were obtained by this method in both superficial and deep burns. The use of grafts should follow the crusting as soon as possible, usually about the tenth day if the burns were deep. The sequence of cover in all burns should be crust, then skin, accomplished within three weeks. The exposure method of treatment had been continued after grafting, with equally satisfactory results, the grafted area being exposed throughout each day.

FESTIVAL SYMPOSIUM ON POLIOMYELITIS

On June 18 a symposium on "Poliomyelitis" was held at 1, Wimpole Street, London, W.1. This was the eleventh of the Festival Scientific Meetings sponsored jointly by the British Medical Association and the Royal Society of Medicine. The Chairman, Dr. F. M. R. WALSHE, opened the symposium by pointing out that the recent increase in the incidence of poliomyelitis had been accompanied by a growth of knowledge on many aspects of the disease.

Poliomyelitis Viruses

Dr. F. O. MACCALLUM said that the poliomyelitis virus was the smallest known virus pathogenic for man, being only 8 to 12 mμ in diameter. Its predilection for the anterior horn cells, as well as its immunological behaviour, distinguished it from related viruses affecting various lower animals.

There were three immunologically distinct types of human poliomyelitis virus, though there might be some degree of overlap of immunity in man. The Lansing strain was capable of being adapted to mice and cotton-rats. It seemed that in areas where sanitary standards were low there was a widespread inapparent infection by this strain in infancy, as shown by serum neutralization tests. It was probable that in this country by 1947 another strain of poliomyelitis virus, of greater virulence than the Lansing strain, had been sufficiently widespread to lead to an epidemic of the disease. There was evidence that in man past infection with the Lansing strain might protect against infection with a more virulent strain.

Native human poliomyelitis virus had recently been successfully cultured in human foetal tissue. The presence of multiplying virus in these cultures was indicated by *p*H changes in the medium which could be prevented by the addition of specific immune serum. This technique thus provided a method of testing for neutralizing antibodies in sera as well as for the growth of virus. The recently identified Coxsackie virus family had grown in number to ten. They were frequently found in association with attacks of clinical poliomyelitis, and Melnick and his colleagues had

found in two patients that there had been a parallel rise in antibodies to both Coxsackie and poliomyelitis viruses during the course of the illness. The Coxsackie viruses were known to cause myositis in experimental animals, and it was possible that in man infection with this group of viruses might be related to the occurrence of muscular pain in the course of the illness.

Symptomatology

Dr. D. MCALPINE pointed out that in an epidemic only 1 to 2% of those infected with poliomyelitis virus became paralysed. Known factors determining the occurrence and the site of paralysis in an infected person included tonsillectomy, muscular fatigue, inoculation, and local infection, in particular of the tonsils and the intestines.

Abortive cases of poliomyelitis showed a clinical non-specific illness resembling influenza, lasting from two to seven days, with malaise, inconstant headache, shivering, mild fever, and a normal C.S.F. The non-paralytic form of the disease showed an extension of the infection to the central nervous system, characterized by muscular pains, stiffness of the back, and paraesthesiae, and accompanied by nystagmus, transitory muscular weakness, alteration in the deep reflexes, and changes in the C.S.F. The onset of paralysis, at times after a symptom-free interval, was accompanied by pain and hyperaesthesia. Variants of the paralytic form included ascending paralysis and the development of an acute myelitis.

Polio-encephalitis was occasionally accompanied by mental symptoms, such as confusion or hypomania, and by drowsiness or more rarely coma. Involvement of the medulla might lead to defects in articulation, deglutition, respiration, and to circulatory failure. Dr. McAlpine concluded with a plea that for the control of epidemics of poliomyelitis emphasis should be shifted to the group of patients not showing paralysis.

Management of the Early Stages

Dr. W. H. KELLEHER considered that the convalescent stage of poliomyelitis was entered when fever, pain, and spread of paralysis had ceased. Abortive cases should be nursed at home and did not require admission to hospital. There was no evidence that lumbar puncture in abortive and non-paralytic cases led to the development of paralysis.

All paralytic cases should be admitted to hospital. There was no specific therapy available against the agent of the disease. Treatment by physiotherapy should aim at the relief of painful spasms by hot moist packs, and at full passive mobility of all joints, with maintenance of correct posture between treatments. Overactivity of the sympathetic system, manifested by bladder and intestinal dysfunction, might be countered by carbachol, and peripheral angiospasm by sympathetic paralysants, such as benzyl imidazoline, or by hot packs.

Early recognition of difficulty with respiration might be aided by spirometry. Complications of treatment in a respirator included respiratory acidosis, hyperventilation atelectasis, pressure sores, acute dilatation of the stomach, and renal lithiasis. With vagal involvement removal of secretions by suction, postural drainage, and the use of a positive-pressure respirator were indicated. The place of tracheotomy was still uncertain. Electrical stimulation of the phrenic nerve might prove the treatment of choice in respiratory disturbance of bulbar origin.

Convalescence

Professor H. J. SEDDON emphasized that recovery from poliomyelitis was a spontaneous affair. The specific changes in the spinal cord had run their course six weeks after the onset of the disease. During this period irritative phenomena might occur: possible mechanisms included a discharging focus surrounding a destructive lesion, a discharging lesion from involvement of the posterior root ganglia, a true myositis in a few cases, and involvement of the sympathetic system. Pain and muscle spasm should be relieved by moist heat or by sympathetic paralysants. Full mobility at all joints should be maintained by passive movements, with the avoidance of prolonged stretching between treatments, and for the latter splints were required chiefly in young uncooperative patients.

Repeated muscle-charting indicated that the time-course of recovery of muscular power extended over a period of eight months. Active exercises from six weeks after the onset were indicated for four reasons: (1) Damage to internuncial neurones might be compensated by a re-routing of voluntary impulses in the cord. (2) A superimposed functional paralysis was not uncommon. (3) Trick movements were of value in the restoration of function. (4) True hypertrophy of healthy motor units could occur.

Professor Seddon entered a plea for simplicity in treatment in the convalescent phase. Electrical stimulation of muscle was useless. Active exercises with springs and slings, and active exercises in the waterbath, were the only two methods required.

Epidemiology

Dr. A. H. GALE recounted some early clinical descriptions of poliomyelitis and quoted the observations of Sir Charles Bell in 1836 on the sequelae of an epidemic affecting young children on the island of St. Helena. In England between 1896 and 1910 the disease, which had previously occurred sporadically, began to appear in small outbreaks. From 1911 to 1946 scattered outbreaks of varying size occurred almost every year, but the years 1926 and 1938 were outstanding. Large epidemics occurred in 1947, 1949, and 1950, and even in 1948 the incidence was abnormally high. There had been a rise in the age incidence in recent epidemics, the age groups 0–4, 5–14, and 15 and over providing almost equal numbers of cases. There was no evident pattern of spread in recent epidemics, and it was difficult to make confident generalizations about the epidemiology of poliomyelitis. Dr. Gale concluded by showing graphs of the weekly notifications of poliomyelitis in this and previous years, and by extending an unanswered invitation to the audience to forecast the trend of notifications for the remainder of the current year.

After a brief discussion, during the course of which the Chairman emphasized the necessity for a precise definition of the terms "abortive" and "spasm," Dr. McAlpine expressed the thanks of the meeting to Dr. Walshe for taking the chair.

Preparations and Appliances

A NEW CARTILAGE RETRACTOR

Mr. J. COLLINGWOOD-STEWART, M.S., F.R.C.S., senior surgeon, Newcastle General Hospital, writes: I have designed the retractor here illustrated for use in operations for the removal of semilunar cartilages from the knee-joint. It has a curved blade to fit the rim of the joint, and also has a shoulder with an acute angle. This

acute angle fits tightly against the tissues at the ends of the incision, and does not slip in and out as is the case with rounded retractors. The retractor has a very bright reflecting surface which gives some additional light when it is in the joint. I use a horizontal incision for these operations, so that a very extensive view of the cartilage is given when the retractor is in position. The apparatus is made by Chas. F. Thackray Ltd., of Leeds.

Correspondence

Laboratory Facilities in General Practice

SIR,—With reference to the discussion on laboratory facilities in general practice at the Royal Society of Medicine (May 5, p. 1012), and the letter from Dr. C. B. Ainscow (June 9, p. 1331), I beg to submit the following observations.

In this urban-rural area some 30 general practitioners have had free access to a full pathology service for nearly four years. They have also had direct access to the radiology department of the hospital for much longer. The result is that patients are investigated by their own doctors. Three things follow. First, the consultant clinics are spared those patients who would otherwise be referred with the sole object of getting an investigation performed. Secondly, a practitioner can refer a patient to one of the consultant staff, having had the opportunity to reconsider his clinical findings in the light of any ancillary investigations done. Thirdly, the consultant whose opinion is sought may see the patient, the *x*-rays, and the pathological findings on the patient's first visit, and is thereby more often in a position to give his opinion on that occasion. A saving of hospital beds results from this and also from the fact that the registrars will often have available *x*-ray and pathological data on the day the patient is admitted. The facilities provided to the general practitioner in fact augment and do not detract from the pathology service to the hospital.

It is perhaps partly because of these facilities that a particular atmosphere prevails in the medical practice of this locality, marked by the sound relationship between the practitioners and the members of the hospital staff and characterized by discussion, which benefits the participants as well as the patients.

I am not clear from Dr. Ainscow's letter whether he considers that practitioners should carry out their own investigations, either individually or as a group. Without wishing to disparage any practitioner who pursues his own particular interests, I think it right to point out that clinical pathology is an analytical and integrative discipline which demands all one's attention and time. It carries with it the responsibility of interpretation, the latter depending on a proper understanding of the method by which a particular result was obtained, and a knowledge of the patient on whom the investigation was done. A history is taken and a clinical examination is performed immediately a patient is referred to the laboratory here, in order that the interpretation of the investigations done may be of the fullest possible value to the patient's doctor. By this method much time can be saved in arriving at a diagnosis, and the practitioner is often helped in selecting therapeutic measures which are specific and rational. No practitioner has, so far as I am aware, taken exception to this procedure, which leaves him sole judge and arbiter of his patient's welfare. The fear of misuse of laboratory services that haunts official minds appears, from my own experience and from all reports, to be groundless. The entertainment of such fears has always struck me as being derogatory to the standards of general practice. It is clear that the provision of laboratory and *x*-ray facilities directly available to probationers leads to invigorated general practice, and is an important factor in the improvement of the relationship between general practitioners and hospitals.

The subject was discussed at the 45th Scientific Meeting of the Association of Clinical Pathologists. It became clear to me then that the problem of providing such facilities for an area containing, say, a population of 500,000, served by 200 doctors, is a different one from that which I have described, where the pathologist can know personally all the practitioners he serves. Nevertheless, our experience on a small scale suggests that the problem should be capable of solution provided that wider recognition is accorded to clinical pathology, in the original sense of that term. The need felt by practitioners in many parts of the country, which exists in spite of the high degree of specialization in all branches of pathology in the teaching hospitals and larger provincial centres, will only be met by pathologists who have maintained an active interest in clinical medicine and who are anxious to pursue the basic sciences of pathology in the closest possible relation to the patient and his doctor.—I am, etc.,

Hemel Hempstead, Herts. G. A. MATTHEWS.

SIR,—I have been following the recent discussion on laboratory facilities in general practice (May 5, p. 1012, and June 9, p. 1331) with considerable interest. Since 1944 the private clinical laboratory in which I act as haematologist has been serving the practitioners in the area and, to judge by the volume of work dealt with, meeting a very real demand.

Since the coming into force of the National Health Service we have been plied with inquiries from general practitioners as to whether our services are available to patients under the scheme. In response to these inquiries we are now putting forward proposals for an arrangement whereby our examinations, at a suitably revised scale of fees, could be ordered by practitioners for their National Health Service patients, the cost to be wholly or partly borne by the Service. Your readers may be interested to learn from this that laboratory facilities are available directly to the general practitioner in parts of the country other than London.

We are hopeful that the representations which we are making will receive favourable consideration, partly because an arrangement under the scheme would obviously be to our advantage in bringing us increased range of work, but also because we feel very strongly that the general practitioner is entitled to a say what investigations are to be carried out on his patients. Dr. C. B. Ainscow in his letter of June 9 mentions the all too prevalent notion in the public mind that the general practitioner is a "signpost to the specialist for anything but the most trivial complaint." The general practitioner, however skilled he may be in the practice of his profession, obviously can do nothing to eradicate this misconception if he is forced to refer any patient for whom he requires even such a straightforward examination as a blood count to a hospital, not because he does not know what requires to be done but because only the hospital clinician has the power to order it to be done.

It is only too well known that the hospitals are overworked and overcrowded. It is high time, therefore, that the general practitioner was allowed to have the satisfaction of diagnosing, investigating, and treating many cases which are well within his scope but which at present find their way to hospital or else, remaining with their own doctors, receive expensive and often unnecessary treatment because those doctors have not the power to obtain confirmation of their diagnoses.—I am, etc.,

Glasgow. ANNE C. V. GREIG.

Diabetes and Pregnancy

SIR,—Dr. J. C. Pease and his colleagues are to be congratulated on the good results they have obtained in the management of their 25 diabetic pregnancies (June 9, p. 1296). They point out that "early induction of labour and prematurity *need* [my italics] not increase the neonatal death rate." Given good team work between the diabetic physician, paediatrician, and obstetrician it is possible to reduce the neonatal death rate of the premature infant to a minimum, as indeed they have so well demonstrated. They mention that many of their babies "proved slow and difficult to establish" and all credit is due to the nursing sister in charge of the infants for the good results. In the larger series of 142 diabetic pregnancies of Peel and Oakley[1] quoted by Pease and his colleagues there was a larger number of neonatal deaths (20) than stillbirths (16), and again in the still larger series of 439 diabetic

pregnancies of White[3] there were 44 neonatal deaths as compared with 34 stillbirths. Few will deny that prematurity does weight the scales against an infant's survival as these larger series demonstrate, and it would be quite wrong to assume that early induction of labour is without its toll of infant life in diabetic pregnancies.

Elsewhere[3] it was shown that in a small series of 22 diabetic pregnancies terminated at the 36th week of pregnancy the foetal salvage rate was 41%, whereas in 23 diabetic pregnancies observed over the same period of time and allowed to terminate spontaneously the foetal salvage rate was 43%. Thus the salvage was approximately the same for the two methods of treatment. Whereas intrauterine death occurred more frequently in the pregnancy that was allowed to proceed, the chance of neonatal death was reduced as compared with the terminated group. Although these numbers are small they would appear to indicate that early termination does not alter the outcome of the diabetic pregnancy as far as the foetus is concerned, but merely changes its death-bed, and of course subjects the mother to the risks of interference. Whatever the lethal factor is in these pregnancies it appears to act on the foetus with increasing intensity to produce intrauterine death in the later weeks of pregnancy. It has been suggested that this lethal factor originates in the maternal anterior-pituitary gland.[4] If an attempt is made to cut short its action by terminating the pregnancy prematurely, an infant is delivered which has already been subjected to its harmful influence and which is therefore less able to withstand its prematurity, and hence more liable to neonatal death than the premature infant of a normal mother. By allowing the pregnancy to continue the chances of intrauterine death are increased, but we have found that in such cases the mother frequently goes into spontaneous labour at 37–39 weeks, so that she naturally cuts short the influence of the lethal factor and yet gives the infant the longest possible time *in utero* compatible with intrauterine survival. The problem therefore is, as stated in the *British Medical Journal*, to find a therapeutic agent which will prevent the harmful effects of this factor and so enable full-time birth to occur.

At University College Hospital since 1947 we have adopted the policy of allowing the diabetic expectant mother to proceed to spontaneous delivery or delivery at term usually by caesarean section on account of the large baby, unless some complication arose necessitating termination for the sake of the mother. In addition she has received hormone therapy in one form or another. We have observed to date 21 diabetic pregnancies with one neonatal death, and three intrauterine deaths occurring at the 33rd, 35th, and 37th week. It is to be noted that two of these intrauterine deaths would not have been avoided by termination of the pregnancy at the 36th week. The neonatal death occurred in an infant weighing 9 lb. 6 oz. (4.3 kg.), the onset of labour occurring at the 38th week spontaneously. The mother developed deep venous thrombosis at the 37th week of pregnancy and was treated with anticoagulants. The baby died from numerous cerebral punctate haemorrhages. The mother subsequently became pregnant and was delivered of a live baby weighing 7 lb. 4½ oz. (3.6 kg.), labour occurring spontaneously at the end of the 37th week. The mother of the infant which died *in utero* at the 33rd week again became pregnant a few months later and was delivered at term of a live infant weighing 8 lb. 13½ oz. (4.0 kg.), the onset of labour being spontaneous. The infant which died *in utero* at the 35th week weighed 8 lb. 13½ oz., and was delivered macerated two days after the absence of foetal heart sounds had been observed, the onset of labour being spontaneous. The mother whose baby died *in utero* at the 37th week had a bad obstetric history. In 1937 she was delivered of a macerated foetus weighing 3 lb. 7 oz. (1.6 kg.), intrauterine death occurring at the 35th week; in 1938 she had a live baby weighing 5 lb. 14 oz. (2.7 kg.) by caesarean section at the 36th week; in 1941 she was delivered by caesarean section at the 36th week of a baby which lived eight hours; in 1942 intrauterine death occurred at the 36th week and she was delivered spontaneously of a macerated foetus weighing 6 lb. 9 oz. (3.0 kg.) at the 40th week; in 1944 caesarean section was performed at the 36th week and a baby weighing 6 lb. (2.7 kg.) was delivered, which died after 14 hours.

One other patient is of interest in this connexion. In 1941 caesarean section was performed at the 36th week of pregnancy. The baby weighed 7 lb. 7½ oz. (3.4 kg.) and lived 12 hours. A year later the performance was repeated and a baby weighing 7 lb. 11 oz. (3.5 kg.) was delivered by caesarean section. This one lived 14 hours. In 1944 caesarean section was again performed at the 37th week. The baby weighed 7 lb. (3.2 kg.) and died after eight hours. Recently she was allowed to proceed to term. Caesarean section was carried out one day after expected date of delivery on account of a large baby and previous caesarean sections. She was delivered of a live baby weighing 11 lb. 6 oz. (5.1 kg.).

I believe that our results likewise demonstrate what can be attained by team work between physician, paediatrician, and obstetrician, and clearly emphasizes the need of an obstetric department being situated in a general hospital where such co-operation can be readily obtained.—I am, etc.

London, W.1. H. H. FOURACRE BARNS.

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SIR,—Drs. J. C. Pease and V. Smallpeice and Professor G. G. Lennon are to be congratulated on their record of 25 consecutive diabetic pregnancies with no maternal deaths, two stillbirths, and no neonatal deaths (June 9, p. 1296). They evidently feel that this admittedly small series refutes the suggestion made in the *British Medical Journal* (1949, **1**, 62), which they quote, to the effect that termination of pregnancy, in order to avoid late intrauterine death in diabetic women, is likely to increase the neonatal death rate. They therefore advocate, *inter alia*, induction of labour not later than the 36th week of pregnancy. Whether pregnancy should be terminated by induction of labour or by caesarean section is a controversy into which I would not care to enter, but I think some comment is justifiable on the propriety of recommending, as they do, the practice of early termination.

In the first place, spontaneous premature labour is not uncommon in diabetic pregnancy (true, it occurred only once before the 36th week in their series of 25 pregnancies); these cases, therefore, are not helped by the recommended procedure, nor will those in which death takes place *in utero* before the 36th week. In the second place, the babies born of diabetic mothers before term are, in spite of their size, generally "bad doers" and it is clear from the authors' report that many of their babies were very difficult to nurse. Obviously the nursing skill and paediatric care for these premature babies must be exceptional at the Radcliffe Infirmary: it is scarcely reasonable to assume that such excellence will be found in most hospitals. The recommended procedure, therefore, counsels delivering a live baby (so as to lessen the risk of being left with a dead one *in utero*), which only nursing skill of the highest order will keep alive. A much larger series of pregnancies, culled from a number of centres where the average of skill is more truly representative of that generally available, would be necessary before it could be accepted that the risks of prematurity in the babies of diabetic mothers are so negligible as to render iatrogenic prematurity the lot of all such babies.

This small series apart, and taking birth statistics generally, the fact is inescapable that prematurity is the cause of nearly half of all neonatal deaths, its incidence rising rapidly as one descends the social scale (see *Papers of the Royal Commission on Population*, 1950, **4**, 15, 17). It is futile, therefore, to suggest that prematurity in the offspring of diabetic mothers is lightly to be encouraged, and the last part of the above-mentioned quotation from the *British Medical Journal* remains true, namely: "To be of real value, oestrogens—*or any other therapeutic agents* [my italics]—must be able to avert late intrauterine death and so enable full-term birth to occur, with its much reduced likelihood of neonatal death."—I am, etc.,

London, W.C.1. G. I. M. SWYER.

3-Hydroxy-2-phenyl-cinchoninic Acid and A.C.T.H.

SIR,—I was interested to read in Mr. Harold Edwards's letter (June 16, p. 1390) of the effects of A.C.T.H. on chronic ulcerative colitis. He quotes that in one centre four consecutive examples of massive bleeding had occurred during treatment of this condition. In view of the reported similarity of response of the suprarenal cortex to both 3-hydroxy-2-phenyl-cinchoninic acid acting in the presence of an intact anterior pituitary gland and A.C.T.H. (Blanchard, K. C., *et al., Bull. Johns Hopk. Hosp.*, 1950, **86**, 83), we have been trying this drug in various conditions which have been ameliorated by A.C.T.H. (see also the paper by Rennie, J. B., *et al., British Medical Journal*, 1951, **1**, 383).

In one patient with chronic ulcerative colitis the immediate clinical response to treatment by oral administration of hydroxy-phenyl-cinchoninic acid was a marked amelioration of symptoms, a fall of temperature to normal, and the passage in a few days of apparently normal stools. After continuing treatment with hydroxy-phenyl-cinchoninic acid for a further three days this patient suddenly developed massive rectal haemorrhage which necessitated transfusion. However, treatment was continued with the drug orally and he is once again passing normal stools. Sigmoidoscopy shows that his colon has improved considerably, although it is far from normal in appearance.

A further feature we have noticed in the treatment of patients with this drug, which increases the parallel between its action and that of A.C.T.H. and cortisone, is that peptic ulcer symptoms increased in severity, possibly due to the increased acid output of the stomach. This, of course, is much like the action of phenyl-cinchoninic acid, which is used experimentally to produce peptic ulcers in dogs (Simonds, J. P., *Arch. Path.*, 1938, **26**, 44) and has produced ulcers in humans when used therapeutically (Bloch, L., and Rosenberg, D. H., *Arch. Path.*, 1932, **14**, 860). There is, as far as I know, no experimental work relating this peptic ulcer producing ability of phenyl-cinchoninic acid to the presence of the anterior pituitary. However, it is of interest in this matter to note that the fore-stomach of the shay rat (Shay, H., *et al., Gastroenterology*, 1945, **5**, 43) seldom develops ulceration in the adrenalectomized rat. This appears to be related to diminution of the volume of gastric secretion which was restored with recurrence of ulceration by cortisone and D.C.A., but most effectively by the administration of normal saline (Madden, R. J., and Ramsburg, H. H., *Gastroenterology*, 1951, **18**, 128).—I am, etc.,

Romford. S. LOCKET.

Haemosiderosis in the African

SIR,—Dr. A. R. P. Walker's letter (April 14, p. 819) raises many points of interest in regard to malnutrition and iron absorption. The immense quantities of iron in the livers of Africans in Johannesburg, which, thanks to the courtesy of Drs. T. and J. Gilman, we have had the opportunity of studying, is an extraordinary phenomenon which as far as we know has no parallel in central and east Africa. The very high incidence of haemosiderosis on the Witwatersrand and its absence in Uganda poses very interesting problems, for similar malnutritional states are seen in both regions. The amounts of iron are so great in the South African livers that comparable states could hardly be missed by those who have studied hepatic pathology elsewhere. In reports from French West Africa[1] and from Kenya[2] no mention is made of marked haemosiderosis. Our colleague Dr. B. G. T. Elmes kindly informs us that he did not encounter the condition in Nigeria. We have never encountered it in Uganda, and, since iron accumulations have not been found at post-mortem examinations at this hospital on natives of tribes in the Southern Sudan, Belgian Congo, Kenya, Tanganyika, and Nyasaland, we infer that it is not common in these regions. We do not know of reports on liver diseases from the Rhodesias, but Gelfand,[3] although he does not specifically mention haemosiderosis in Southern Rhodesia, merely quotes the findings from Johannesburg, and we infer that it is not common in Rhodesia, and neither does Blaine[4] mention it in a brief report. Dr. Walker states that we do not know its geographical distribution in South Africa. Yet we understand that workers from the Rhodesias and Nyasaland figure largely in the Witwatersrand labour forces.

Over most of the area between Kampala and Johannesburg there is widespread malnutrition, and, although the staple carbohydrate varies from area to area, many tribes subsist largely on maize, and drink, *inter alia*, fermented maize liquors. Although locally an aluminium pot is preferred as a cooking vessel, paraffin cans are widely used, as are iron cooking pots. We have no figures, however, for iron intake; anaemia is common, especially in association with hookworms, and the majority of our cases come from malarious areas. The effect of malaria in tending to promote iron deposition in the liver is perhaps counteracted by the abstraction of iron by hookworms, and perhaps the hookworm protects our local inhabitants from haemosiderosis, though we can hardly credit it.

We would suggest that a knowledge of the geographical distribution of haemosiderosis between Kampala and Johannesburg, with delineation of the areas where the incidence begins to rise, might be an important step in establishing the aetiology of haemosiderosis. Such a survey, if organized, might not prove too difficult to carry out, as, thanks to the interest taken in yellow fever by the Rockefeller Foundation, viscerotomes are available in many hospitals throughout this vast region. Use of these instruments in areas where complete necropsies are not possible could establish the geographical distribution of haemosiderosis as well as other forms of liver disease, and not only of liver disease, for where a viscerotome is available many organs can be sampled through very small incisions.—We are, etc.,

Mulago Hospital, Kampala, Uganda. J. N. P. DAVIES. H. C. TROWELL.

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Absorption of Hexamethonium

SIR,—In his letter (June 9, p. 1331), Dr. S. Locket suggests that, when hexamethonium bromide is administered by the oral route, only 4–5% is absorbed. This suggestion is apparently based only upon the quantity excreted in the urine, determined by the method described by E. J. Zaimis (*Brit. J. Pharmacol.*, 1950, **5**, 424). G. E. Milne and S. Oleesky (*Lancet*, 1951, **1**, 889) drew a similar conclusion. It is difficult to understand how any conclusion can be arrived at upon the extent of oral absorption in the absence of any method of estimation of the serum levels. Hexamethonium is not a stable compound; we have seen ampoules of the iodide prepared a year previously which spontaneously became subject to yellowish-green discoloration with marked loss of activity. Until proved otherwise it is probably unwise to assume that some of the drug is not metabolized. It is not chemically unrelated to naturally occurring substances. Milne and Oleesky record that, with an oral dose of 3 g. per day, 19–30% was recoverable in the faeces of one patient. Might this not suggest the absorption and detoxication of a substantial part of the dose?

The oral route involves a slower absorption and greater possibility of modification in the liver. During the last 18 months of therapeutic application of hexamethonium in hypertension, in oral dosage of 2–3 g. total per day, we have had evidence of absorption of an adequate amount to produce a hypotensive action in many patients. Admittedly the activity by this route is not so immediate and precise as when hexamethonium is administered parenterally as described by F. H. Smirk and K. S. Alstad (*British Medical Journal*, 1951, **1**, 1217), but it has been sufficient to occasion

improvement of many ambulant patients with hypertension, with a comparative convenience of administration. A. W. Kay and A. N. Smith (*British Medical Journal*, 1950, **2**, 807), who were the first to use hexamethonium orally, determined that 500 mg. by mouth produced an effect upon gastric secretion and motility equal to that of 100 mg. intramuscularly. We have confirmed this finding on many occasions in gastric secretion. We have found this dosage ratio to obtain approximately in the maintenance treatment of hypertension, and it is reasonably in accord with the relative biological toxicities prepared by one of the manufacturers of this drug (May and Baker, Ltd.), which are for the bromide salt in mice 0.026 mg. per g. intravenously and 0.70 mg. per g. orally, approximately 3 : 1.

We are in agreement with Dr. Locket that there is a greater tendency to constipation when hexamethonium is administered orally. However, during treatment of some 50 patients at this hospital, there were only two instances of paralytic ileus. These occurred at the beginning of our experience. A mild laxative such as liquid paraffin has since been routinely prescribed to all patients receiving hexamethonium and there has been no further instance of this complication, which was recorded by A. Campbell and E. Robertson (*British Medical Journal*, 1950, **2**, 804).—We are, etc.,

J. GIBSON GRAHAM.
A. CAMPBELL.

Paisley.

Electrophrenic Respiration in Asphyxia Neonatorum

SIR,—It was with considerable interest that my colleagues and I read the report of Dr. K. W. Cross and Mr. P. W. Roberts, and the related annotation, in the May 12 issue of the *British Medical Journal* (pp. 1043 and 1070) on the subject of electrophrenic respiration in asphyxia neonatorum. We are in a position to appreciate keenly the organizational effort as well as the investigational endeavour that must have gone into this study and were highly gratified that a method in which we have been so interested seems to have found some area of usefulness as applied to the newborn infant. It seems worth while to address this to you both for the purpose of expressing the above and of mentioning several related observations pertinent to the above report.

In preparation for a study on electrophrenic respiration in neonatal asphyxia we have, with the encouragement of Dr. Clement Smith, been training several of the house-officers of the Boston Lying-in Hospital in the use of the electrophrenic respirator. We have produced effective ventilation in 28 consecutive infants between the ages of 8 and 48 hours. None were in need of respiratory assistance. The programme was undertaken in support of our view that an emergency procedure, and especially electrophrenic respiration, is best practised at some length before the user brings the method to an actual emergency situation.

We can support the observation of Cross and Roberts that newborn infants require an appreciably higher voltage than adults for effective phrenic stimulation. It is well known that myelinization of motor nerves is far from complete in the newborn infant and that, in general, the electrical threshold of excitability of nerve fibres is inversely proportional to their degree of myelinization. It is not surprising, therefore, that a newborn infant's motor nerve requires a higher potential for the excitation of a propagated impulse. This is, of course, of theoretical interest, but of little practical importance, since in practice one simply increases the potential until a phrenic motor response is obtained. One scarcely bothers even to observe the potential used, since it is not the electrical threshold but diaphragmatic descent in which one is interested. Needless to say, the maximum output of which the electrophrenic respirator is capable has been held well below that capable of causing injury. It was with some surprise that we noted that Cross and Roberts did not obtain inhibition of spontaneous respiration in infants as they did in adults until we considered the rate of respiration they were using. The factors involved in the suppression of spontaneous respiration have been clearly set forth (Paul O. Chatfield and Stanley J. Sarnoff, "Role of Pulmonary Proprioceptive Reflexes in Suppression of Spontaneous Breathing During Electrophrenic Respiration," *Amer. J. Physiol.*, 1950, **163**, 118). It is no more reasonable to expect that their rate of 18 per minute would inhibit a newborn infant's spontaneous breathing than it would be to expect a rate of nine per minute to do so in the adult. Suffice it to say that clear suppression of spontaneous respiration was obtained by us in each of the 28 infants in which electrophrenic respiration was tried. Rates of between 30 and 45 per minute were used. We are unaware of any significant hazards to be feared from moderate overventilation for the periods of time used by Cross and Roberts in their study.

The apparatus used by Cross and Roberts was, we presume, constructed with a view to yielding important and needed data in addition to producing artificial respiration. However, as pointed out in the annotation mentioned above, the various electrical designations may prove confusing to the average physician. The physiological advantages of this method over positive pressure breathing are manifest. Whether or not it becomes a generally useful method revolves plainly and simply around the problem of feasibility. It is for this reason that the clinical apparatus now commonly in use in this country has only non-electrical designations—e.g., "Rate," "Depth," and "Distribution" (long or short inspiration) and an off-on switch. Knowing how many amperes or volts are being applied contributes absolutely nothing to the ability of the user to produce effective ventilation in either the newborn infant or adult. When first starting to use electrophrenic respiration by external stimulation, we had the subject's head turned away from the side on which stimulation was to be applied, and indeed it was this positioning which Dr. Cross saw demonstrated by us in 1949 before the British Physiological Society, so that he was entirely justified in assuming that that was what had proved most useful in our hands. Since then, however, we have observed that if the head is held straight forward in the anatomical position this has the effect of relaxing the sternocleidomastoid muscle and permits the electrode to be placed more effectively in relation to the motor point of the phrenic nerve on the anterior surface of the scalenus anticus muscle. If one uses this positioning of the head and a somewhat smaller electrode than that used by Cross and Roberts it is possible to elicit solely a diaphragmatic response without the activation of muscles supplied by nerves of the cervical or brachial plexus.—I am, etc.,

Harvard University. STANLEY J. SARNOFF.

The Case for the Billroth I Gastrectomy

SIR,—I should like to say a small word both in support of Mr. Brendan Hickey's (April 14, p. 818) observations and those of Mr. Lang Stevenson (June 9, p. 1329) on the subject of the Billroth I gastrectomy for both gastric and duodenal ulcer. It has always seemed to me purely on anatomical grounds to be the sounder operation, because at the end of the operation you have a gastro-duodenal tract which approximates to the physiological stomach in its continuity. I believe that there are a number of reasons, and rarely adequate ones, for the unpopularity of this operation as compared with the Polya and Hofmeister–Finsterer resections. The first is that the operation is more difficult because the greatest caution must be observed in mobilizing the first part of the duodenum, and this may be both difficult and hazardous in the presence of a penetrating ulcer. If this ulcer extends for some distance along the first part of the duodenum the posterior lip of the duodenal surface to be anastomosed is devoid of peritoneum, and this may introduce a fear of leaking from the subsequent junction. Mobilization of the second part of the duodenum of course presents no difficulties. Another reason for abandoning the Billroth operation is fear of stenosis at the junction with greater curvature of the stomach.

I submit that this fear is unwarranted if the interrupted stitches in two layers are employed. Personally I use fine linen thread, but I think the material used is of less importance than the avoidance of continuous sutures. I have done more than 200 gastric resections by this method and have never had either bleeding or leaking at the site of the junction. I must confess that I am not an enthusiast for combining vagotomy with gastric resection, on the principle that if the vagotomy is done temporary atony and dilatation of the stomach may be expected, and I feel that this might throw a strain on the suture line. A Ryle's tube for the first four days after operation might, I suppose, alleviate this, but I always allow my gastrectomies to take fluids by mouth within 12 hours of operation; and I like to think that the stomach is emptying itself in the normal way.—I am, etc.,

London, W.1. GEOFFREY PARKER.

Potassium Bromate Poisoning

SIR,—I read with interest the article on potassium bromate poisoning by Dr. A. Parker and Dr. Johnston R. Barr (June 16, p. 1363), as I had a similar case about three weeks ago, unfortunately before the publication of their article. The patient, a boy of 4 years, weighing 30 lb. (14 kg.), had found a packet of "hair neutralizer," some of which he had sprinkled into a cup of milk and then swallowed. The amount was unknown, but, judging by the amount left in the packet, it could not have been very much. The child had been put to bed in the evening, when he had appeared normal. Later he had woken complaining of abdominal pain and vomiting. When seen, about four hours had elapsed from swallowing the neutralizer. The child was pale and fretful, and repeatedly vomited small amounts of blood-stained mucus, the staining being bright red. An immediate stomach washout was given, using sodium bicarbonate. The washout was continued until no mucus or blood was obtained. Then half a pint (284 ml.) of cream, with an egg yolk whipped up in it, was given to him, partly by mouth, partly by Ryle's tube, as he found it too rich. The child was drowsy but resented any interference sufficiently strongly to make an intravenous injection of picrotoxin impracticable, so 5 mg. of D-amphetamine sulphate was given with the cream to counteract the drowsiness. About half the cream was retained. The child remained drowsy for the next 48 hours, during which time the pulse, at first 160, fell slowly to 100, then rose to 140, and then gradually settled to 100. He then became brighter and more normal, the pulse rate, however, varied between 140 and 80 until the fourth day. Methaemoglobin was never present in detectable quantities and there was never any anuria. The child was discharged on the twelfth day.—I am, etc.,

Chesterfield. G. I. BENSON.

POINTS FROM LETTERS

Successful Homograft

Dr. F. C. ENDEAN (London, S.W.1) writes: The leading article on homografts in your issue of May 26 (p. 1157) recalls a case I grafted successfully. Briefly, an Australian volunteer ordinary seaman was put ashore at Singapore some time during 1917 for circumcision. A week after the operation the sites of the stitches necrosed and the condition extended until the entire skin covering of the body of the penis was destroyed. A skin graft taken from the patient's thigh failed. The local condition was all against grafting. Then the idea suggested itself to me to try a homograft from a boy due to be circumcised. After the operation I dissected off the inner layer of the boy's prepuce and cut it into four pieces and stitched these in a row downward to the right corpus cavernosum. A saline drip was used to keep the site of operation as clear as possible. Before the tenth day the lower three grafts turned black and fell away, but the top graft, although shrivelled and black, was still adherent on the 14th day. The next day the last graft came off and a magnifying glass revealed a small white speck which eventually grew to cover the whole affected area. The patient made an uneventful convalescence and returned to duty. After the war he wrote from Australia stating that everything was perfect.

Obituary

E. H. HARRIES-JONES, M.D.

Mr. E. H. Harries-Jones, ophthalmic surgeon to the Northampton General Hospital for 50 years, died in Northampton on June 7, aged 77. Evan Harries Harries-Jones was born at Rhyl. He was Welsh to the bone and was proud of it, speaking the Welsh language fluently. As a youth he was apprenticed to Dr. Hughes, of Ruthin, and his academic medical training was taken at Edinburgh and Dublin. After graduating M.B., C.M. in 1897, he proceeded M.D.Edin. in 1900. His early work in surgery of the eye was done in the Birmingham Eye Hospital, where he occupied every residential post, from junior house-surgeon to resident surgical officer. In 1901 he was appointed as the first honorary ophthalmic surgeon to the Northampton General Hospital. His success was great, and he became a leading figure in the public and professional life of the town. In later years he was one of the founders of the Oxford Ophthalmological Congress and was also President of the Midland Ophthalmological Society. Secretary of the South Midlands Branch of the B.M.A. from 1901 to 1924, he was its President in 1927–8. He made several important contributions to the literature of his specialty.

W. M. R. writes: Conditions were difficult when "H.J." started in Northampton, since there were no ophthalmic beds and no special out-patient department. I remember him telling me with a twinkle in his eye that he was amused by the large number of cataracts in the left eye which he found on the waiting-list for operation when he took over, but none for the right eye. This he attributed to the fact that few general surgeons are ambidextrous. In 1924 one of his private patients, in order to help others similarly afflicted and as a token of gratitude to "H.J.," presented to the General Hospital those fine in-patient wards and out-patient buildings, complete with operating-theatre, private rooms, etc., which are known as the Singlehurst Block. This new department was opened by our present King, who was then Duke of York. It was in these buildings that Harries-Jones subsequently did all the fine work for which Northampton and its area are so duly proud and thankful. In 1926 he was joined by Mr. S. H. G. Humfrey. Together, by strenuous work, these two maintained a thoroughly efficient ophthalmic service for this extensive area until the coming of the National Health Service Act.

Harries-Jones had a national reputation amongst ophthalmic surgeons, with whom he kept in close touch at their annual and other meetings. His life, however, had other interests in spite of the pressure of professional duties. From his youth Freemasonry had an intense attraction. As the years went by he succeeded to higher and higher honours. He became Provincial Prior of the Order of Knights Templar, which was his favourite Order, and in 1945 reached the peak as Provincial Grand Master for the Province of Northants and Hunts. As a colleague Harries-Jones had the charm and loyalty which transform a hospital staff into a happy family. His staunch adherence to what was ethically sound never allowed him to be found at a disadvantage. He was loved by us all. He was, moreover, a man of reading, and historical works had

a large claim on the time he devoted to this form of recreation. Above all, he had that sense of humour which made him popular in whatever grade of society he may have been found. He married Miss M. B. Manfield, daughter of Mr. James Manfield, the founder of the Manfield Orthopaedic Hospital, by whom he had one son and one daughter, who is now married to Mr. S. H. G. Humfrey, his colleague and successor. So has ended a life devoted to helping others, whose memory will linger till time shall bring forgetfulness.

Dr. J. M. TAYLOR died suddenly at Cymmer, Port Talbot, Glamorgan, on June 2, after being in practice there for 39 years. His loss will be felt throughout the whole of the South Wales Valley, where he was very greatly loved and respected. James McKane Taylor was born at Dervock, in N. Ireland, and studied medicine at Edinburgh University, where he graduated M.B., Ch.B. in 1910. After holding resident appointments at the General Hospital and the Queen's Hospital, Birmingham, he went on to Manchester to study gynaecology and midwifery at the Cheetham Hospital. He then settled down at Cymmer, where, employing his great energy and capacity to full advantage, he carried on a most successful practice for the rest of his life.

J. B. H. writes: "Tip" Taylor was a real, true Irishman. A certain roughness of speech and manner really hid a kindness he was very shy of expressing. To see and hear him rate someone, and then suddenly observe his rugged face break into a smile, was like seeing the sun come out of a dark cloud. His many patients will, I know, never forget him; they were his friends for whom he did so much. He never had an assistant, and, until the beginning of the last war, he never had a car, but did all his rounds on foot or on a bicycle. Having no hobbies, he lived for his work and family—his wife, two sons, and two daughters—to whom our deepest sympathy goes.

Dr. L. P. GRAY, who was in general practice for a number of years in Epsom and Chingford, died in London on June 5, aged 48. Leo Patrick Gray graduated M.B., Ch.B. at Glasgow University in 1928. After holding posts as house-physician and anaesthetist at the Victoria Hospital, Burnley, and resident medical officer at the Warwick County Mental Hospital, he went into general practice. He was always interested in industrial health, and in 1943 was appointed works medical officer of Vickers-Armstrong, but increasing ill-health compelled him to retire altogether from medical work a few years ago.

Mr. Colm Brogan writes: Dr. Gray maintained a most lively interest in all medical problems, and it is probable that in his last years of professional inactivity he exercised more influence and contributed more to the welfare of the medical profession than in the years when he was fully engaged as a doctor. From boyhood, Leo Gray had been condemned to struggle against the disadvantage of a seriously affected heart. He was a man of immense physical and mental vigour, with all the qualities of leadership and a most unusual integrity. Granted full health, he would have made a deep impression in medical and perhaps in public life. Even with his heavy handicap he won the respect and affection of a wide variety of friends and colleagues. Among the numerous expressions of regret and loss which followed his death, it was notable how many came from people who had first made his acquaintance after his retirement from the practice of medicine. These were a remarkable tribute to a character of singular force and fortitude and integrity.

His many friends and old patients will be grieved to learn of the death of Dr. CHARLES MELVILLE YOUNG, which occurred in the early hours of June 8 at his residence at Rickmansworth. The eldest son of Andrew Young, valuer to the London County Council, he was born in London on Christmas Eve in 1875 and educated at St. Albans Grammar School. He studied medicine at Aberdeen University, where he graduated M.B., Ch.B. in 1900. Thereafter he filled the posts of assistant medical officer and casualty officer at the London Temperance Hospital before he settled in practice in South-West London near Wandsworth Common. There he rapidly built up a large practice and was also elected honorary anaesthetist to the Bolingbroke Hospital, to which institution he gave devoted service for more than twenty years. He was at one time president of the South-West London Medical Society. During the war of 1914–18 he served in France in the R.A.M.C., being attached to the 91st Field Ambulance. In 1925 he was appointed medical officer to the Royal Masonic School for Girls at Wandsworth, and in 1934, when the school was removed to Rickmansworth, Dr. Young, who was already feeling the strain of his extensive practice, decided to confine his attention to the work at the school. He therefore gave up his general practice, took a house at Rickmansworth, and devoted all his skill and strength to the good of the hundreds of girls at the Royal Masonic School. At the time of leaving Wandsworth he was senior anaesthetist to the Bolingbroke Hospital, and when he left he was elected consulting anaesthetist. Dr. Young was not a strong man, and during the last few years it had been evident that his strength was failing. In spite of anginal attacks he worked on till last year, when he felt compelled to give up all work. It was a great wrench for him to sever his association with the Masonic School. Towards the end he bore very severe pain with great fortitude. A largely attended memorial service was held at the Methodist Church, Rickmansworth, on June 17.

V. Z. C. writes: The bare outline of Dr. Young's life gives but little idea of his modest but great personality. He had the true vocation of a doctor. His life was in his work and he lived for his patients. No trouble was too great and no time was sacrosanct when the good of the patient was in question. Being without guile himself, he found difficulty in seeing anything but good in others. These qualities or faculties endeared him to his patients and well fitted him to be the medical officer of the large Masonic School. He was fond of children, and found great satisfaction and happiness in looking after the welfare of many generations of girls at the school. He was certainly one of the best doctors both as to ability and character that I have ever known. In 1907 Dr. Young married Beatrice Pertwee, and his family life was exceedingly happy. Everyone's sympathy will go out to his widow and daughter.

Medical Notes in Parliament

Russian Crab Meat

Mr. MAURICE WEBB said in reply to questions on June 18 that he had seen Press reports about cases of food-poisoning alleged to have been caused by the consumption of Russian crab meat. The quantity covered by the last contract for this commodity was about 800 tons, all of which had been released. On arrival in this country the goods were examined in the usual way and found to be in sound and perfect condition. The Public Health Laboratory Service had examined the remainder of the food in the can that was thought to have been the cause of cases of illness, but as this examination did not take place until some time after the can had been opened the results were inconclusive. But an examination of 20 unopened cans of the same batch showed that they were all perfectly sound. He felt that hon. Members and the public could be reassured about the quality of this product and the efficiency of the routine tests.

Tuberculosis in Scotland

Miss HERBISON on June 19 told Mr. MALCOLM MACPHERSON that the improvement which took place in the tuberculosis situation in Scotland during 1950 had continued in 1951. In the first quarter of 1951 there were 723 deaths

from all forms of tuberculosis, as compared with 826 in the first quarter of 1950. For the first 23 weeks of 1951 there were 4,489 new cases notified, as compared with 4,678 in the corresponding period of 1950. Apart altogether from beds in Swiss sanatoria the number of beds available in Scottish hospitals for the treatment of tuberculosis increased by 176 in the first quarter of 1951. She added that while this trend was most encouraging it was no reason for relaxing efforts. All concerned should give first priority to the improvement of services for the prevention and treatment of tuberculosis in Scotland.

Medico-Legal

£2,453 DAMAGES FOR INJURED FINGERS

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

The Court of Appeal, allowing an appeal[1] by Mr. D. T. Thurogood against a judgment of Mr. Justice Devlin, entered judgment in his favour against his employers for £2,453 as damages for injuries by fracture and laceration to his fingers which were caught in the blades of an electric fan. Leave to appeal to the House of Lords was given to the employers.

The fan was normally run to ventilate a room in the employers' factory used for one of the processes in making margarine, but at the time of the accident it had been moved to the electrical section in a different part of the factory for test. Mr. Thurogood, in the course of his duty as electrician, was feeling the fan motor to check for vibration and heat when the accident happened.

Mr. Justice Devlin had held that the electrical section was a separate "factory" within the meaning of the Factories Act, 1937, and that because the fan was not part of the machinery of that separate factory but had been taken there for repair it was not required under the Act to be securely fenced. Accordingly he held that the employers were not liable to Mr. Thurogood for breach of statutory duty to fence. He also held that they were not liable for negligence at common law.

Lord Justice Cohen and Lord Justice Asquith, in allowing the appeal, both took the view that the electrical section was not a "separate factory" within the meaning of the Act, that the employers were obliged to ensure that dangerous machinery there was securely fenced, and that they were therefore liable for breach of statutory duty. They also held that the employers were liable at common law. At most Mr. Thurogood, in getting his fingers into the fan, had been guilty of inadvertence or forgetfulness which did not amount to contributory negligence, and the employers ought to have anticipated that unless they took proper precautions there would probably be an accident.

The Lords Justices accordingly allowed the appeal on both grounds, and Lord Justice Birkett concurred.

[1] *The Times*, March 3.

Universities and Colleges

UNIVERSITY OF OXFORD

Dr. E. G. T. Liddell, Fellow of Magdalen College, has been elected a member of the Halifax House Committee.

Dr. Janet M. Vaughan, Principal of Somerville College, has been reappointed as a delegate of the University Museum for three years from the first day of Michaelmas Term.

UNIVERSITY OF CAMBRIDGE

In Congregation on June 7 the honorary degree of Sc.D. was conferred on Sir John Sebastian Bach Stopford, M.D., F.R.C.P., F.R.S., Vice-Chancellor of and Professor of Experimental Neurology in the University of Manchester, and on Professor Albert Michotte van den Berck, Director of the Experimental Psychology Laboratory in the University of Louvain.

In Congregation on June 9 the degree of M.D. was conferred on D. Rice and R. F. Hobson.

UNIVERSITY OF GLASGOW

On June 15 the degree of M.D. was conferred upon R. N. Sinclair.

UNIVERSITY OF LONDON

The following have been appointed, or nominated for appointment or reappointment, as representatives of the University on the governing bodies indicated in parentheses: Professor S. J. Cowell and Professor Esther M. Killick (King's College of Household and Social Science); Dr. J. Purdon Martin (National Hospital for Nervous Diseases); Professor M. E. Delafield (Public Health Engineering Advisory Committee).

The following have been recognized as teachers of the University in the subjects indicated in parentheses: *Institute of Laryngology and Otology:* Mr. N. Asherson and Mr. M. P. Ellis (Oto-rhino-laryngology). *Middlesex Hospital Medical School:* Miss Diana J. K. Beck (Surgery). *St. George's Hospital Medical School:* Dr. J. W. D. Bull (Radiology) and Dr. E. Landau (Anaesthetics). *Institute of Obstetrics and Gynaecology:* Miss Amy M. Fleming (Obstetrics and Gynaecology) and Dr. R. M. Haines (Pathology).

The following, who are already recognized teachers at undergraduate medical schools, have been also recognized as teachers at the Institute of Obstetrics and Gynaecology in the subjects indicated in parentheses: Mr. A. B. Evans (Obstetrics and Gynaecology) and Dr. P. M. F. Bishop (Medicine).

Dr. G. W. Hayward resigned the post of Reader in Medicine and Assistant Director of the Medical Professorial Unit at St. Bartholomew's Hospital Medical College as from March 31.

The following awards of medical entrance scholarships have been made on the results of the London Inter-Collegiate Scholarships Board's examinations in February: *Bucknill Scholarship, University College*, M. T. Morgan (Leyton County High School).

Dr. Charles Enrique Dent has been appointed to the University Readership in Medicine tenable at University College Hospital Medical School from October 1.

The following scholarships at the Royal Free Hospital School of Medicine have been awarded for 1951–2: *Mabel Sharman-Crawford Scholarship* (£40 per annum for four years), Miss M. C. Underwood; *MacIntyre Evans Scholarship* (£75 per annum for four years), Miss A. M. Maclean; *Elizabeth Garrett Anderson Scholarship* (£40 per annum for four years), Miss R. L. Dart; *Dr. Margaret Todd Scholarship* (£40 per annum for four years), Miss A. de la C. Davies; *Florence Hughes Scholarship* (£40 per annum for three years), Miss N. A. Lloyd-Jacob; *A. M. Bird Scholarship for Clinical Studies* (£40 per annum for three years), Miss C. M. Oakley.

Mr. P. H. Mitchiner has been appointed Deputy Vice-Chancellor as from September 1 for the university year 1951–2.

Applications are invited for the William Julius Mickle Fellowship, of the value of approximately £230, which is awarded by the Senate to the man or woman who, being resident in London—i.e., within the administrative area of the London County Council—and a graduate of the University, has in the opinion of the Senate done most to advance medical art or science within the preceding five years. Applications must be received by October 1 and further particulars should be obtained from the Academic Registrar, Senate House, London, W.C.1.

ROYAL COLLEGE OF PHYSICIANS OF IRELAND

On June 14 the Honorary Fellowship of the College was conferred on Professor Edward Joseph Conway, F.R.S., Professor of Biochemistry and Pharmacology at University College, Dublin. After the ceremony Professor Conway delivered an address on "Science and the Physician."

The following Members were admitted to the Fellowship of the College on June 1: M. L. F. Drury, P. D. J. Holland, A. F. Kennedy, J. P. Malone, S. P. O'Toole, B. E. R. Solomons, F. S. Stewart, E. W. L. Thompson.

The following were admitted to the Membership of the College on June 1: A. D. H. Browne, E. M. Cheffins, A. L. Jones, S. G. McComb, T. C. Milliken, N. B. O'Donohoe, D. G. Simpson, H. B. C. Wallace.

ROYAL COLLEGE OF SURGEONS IN IRELAND

On June 15 the Fellowship of the College was conferred on the following successful candidates: J. R. Evans, J. E. F. Coolican, J. Campbell-Reid, M. J. P. McCormack, J. McCabe.

At a meeting of the College held on June 4 Professor William Pearson was elected President of the College and Mr. M. P. Burke Vice-President for the ensuing year.

INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles for the week ending June 9 (No. 23).

Figures of notified *cases* are for: (*a*) England and Wales (London included). (*b*) London (administrative county). (*c*) Scotland. (*d*) Northern Ireland. (*e*) Eire. Figures of *births and deaths* and of *deaths* recorded under each disease are for: (*a*) The 126 great towns in England and Wales (London included). (*b*) London (administrative county). (*c*) The 16 principal towns in Scotland. (*d*) The 10 principal towns in Northern Ireland. (*e*) The 13 principal towns in Eire. A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, Northern Ireland, and Eire, the Ministry of Health and Local Government of Northern Ireland, and the Department of Health of Eire.

Disease	1951 Week Ending June 9					1950 Corresponding Week					1942–50 England & Wales Corresponding Week		
	(*a*)	(*b*)	(*c*)	(*d*)	(*e*)	(*a*)	(*b*)	(*c*)	(*d*)	(*e*)	Highest	Median	Lowest
Diphtheria	37	3	15	2	2	73	6	9	1	—	634	304	73
Deaths	—	—	—	—	—	—	—	—	—	—			
Dysentery	682	145	101	6		353	22	134	2	2	426	127	53
Deaths		—		—					—				
Encephalitis, acute	—	—	—	—		5	—	—	—		5	3	—
Deaths		—			—		1			—			
Erysipelas			11	2	3			13	3	10			
Food-poisoning	59	19		—		191	31		3				
Infective enteritis or diarrhoea under 2 years				12	16					19			
Deaths	8		3	4	—	22		2	1	2			
Measles*	14,746	420	467	296	201	10,712	613	960	118	291	13,525	8,463	3,078
Deaths		—	—	—	1		—	—	—	—			
Meningococcal infection	53	1	17	2		42	5	18	2	2	136	49	28
Deaths		—	—				—	—					
Ophthalmia neonatorum	40	—	11	1		47	5	11	—		98	60	45
Pneumonia, influenzal	372	12	8	6		480	23	4	6	—	738	480	416
Deaths (from influenza)†	9	3	—	—	—	9	—	2	—	1			
Pneumonia, primary			150					170					
Deaths	139	22		5	7	186	20		4	7			
Poliomyelitis, acute :													
Paralytic	32	2	4	—		79	6	8	1	8	79	9	5
Non-paralytic	20	—			—								
Deaths§	4	1				7	—		—				
Puerperal fever			6				—	9					
Puerperal pyrexia‖	84	6	6	—	2	84	1	7	2	—	179	128	84
Scarlet fever	972	102	144	19	47	846	62	140	49	55	2,008	1,090	730
Deaths		—	—	—	—			—	—	—			
Smallpox	—	—	—	—		—	—	—	—				
Deaths				—					—				
(1) Tuberculosis, respiratory			147	67				211	54				
(2) Tuberculosis, non-respiratory			28	15				45	2				
(1) Deaths	111	18	25	7	7	183	28	31	5	9			
(2) Deaths		2	2	1	5		5	4	1	4			
Typhoid fever	7	—	—	1	—	9	1	1	2	1			
Deaths¶	—	—	—	—		1	1	—	—		33	11	4
Paratyphoid fever	15	1	—	—		7	1	1 (B)	—				
Whooping-cough	3,275	207	351	63	39	3,437	168	358	49	135	3,437	2,050	1,033
Deaths	—	—	—	—	1	5	—	2	—	—			
Deaths (0–1 year)	224	32	22	12	11	239	33	37	13	14	473	289	239
Deaths (excluding stillbirths)	4,378	687	578	98	159	4,779	731	584	125	144	4,779	4,130	3,796
Annual death rate (per 1,000 persons living)			11·7					11·7					
Live births	7,358	1,283	986	257	497	7,951	1,269	928	209	362	9,613	7,418	5,462
Annual rate per 1,000 persons living			19·9					18·6					
Stillbirths	186	23	17			177	24	32			256	219	177
Rate per 1,000 total births (including stillborn)			17					33					

* Measles not notifiable in Scotland and returns are approximate. † Includes primary form for England and Wales, London, and N. Ireland. § The number of deaths from poliomyelitis and polio-encephalitis for England and Wales, and London (administrative county), are combined. ‖ Includes puerperal fever for England and Wales and for Eire. ¶ Deaths from paratyphoid fever are combined with those from typhoid fever.

Vital Statistics

Poliomyelitis

Poliomyelitis notifications in the week ending June 16 were as follows (figures for the previous week are in parentheses): paralytic 25 (32), non-paralytic 25 (20); total 50 (52). The Table below compares the current year with the four previous years in respect of notifications in England and Wales in weeks 1–13 (in which it may be assumed that many cases represent the aftermath of the preceding year) and weeks 14–24.

Year	Total in Year	Weeks 1–13		Weeks 14–24		Remarks
		Actual	Percentage of Total for Year	Actual	Percentage of Total for Year	
1947	9,335	125	1·3	160	1·71	Epidemic year
1948	2,239	418	18·7	196	8·75	Post-epidemic year
1949	6,960	248	3·6	173	2·49	Epidemic year
1950	8,766	512	5·8	411	4·69	Post-epidemic and epidemic year
1951	?	339	?	302	?	?

Up to and including the week ending June 9 the overall notification rate for England and Wales was 1.34 per 100,000. Regionally the highest rates were in the midland and south-west regions—2.09 and 2.08 per 100,000 respectively—and the lowest in the north-western and the E. and W. Ridings—0.97 and 0.9 per 100,000 respectively.

In weeks 1–23 some districts with large numbers of notifications were as follows (rates per 100,000 in parentheses): Birmingham C.B. 37 (3.3), Orpington U.D. 18 (30.4), Flint M.B. 7 (49.4), Barnsley C.B. 6 (8.0), and St. Austell R.D. 6 (38.2).

Road Accidents in April

Road casualties in Great Britain during April totalled 16,049, compared with 14,005 in the corresponding month last year. Deaths numbered 379, compared with 349; seriously injured 3,930, compared with 3,458; and slightly injured 11,740, compared with 10,198. Total casualties in April, 1939, were 18,597.

Infectious Diseases

In England and Wales during the week ending June 9 the numbers of notifications of measles fell by 884, of dysentery by 71, and of scarlet fever by 71, while rises were recorded for whooping-cough 57 and acute poliomyelitis 24.

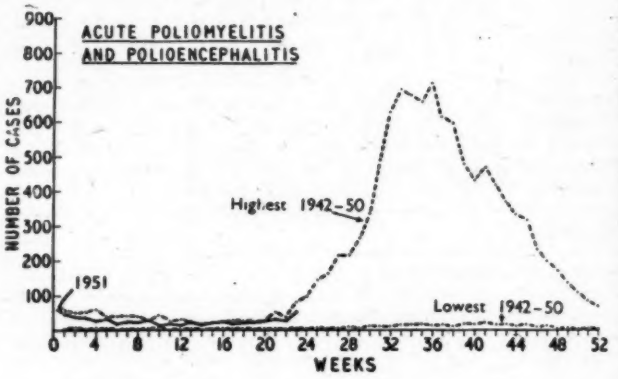
The largest decreases in the incidence of measles were Yorkshire West Riding 173, Staffordshire 169, Warwickshire 131, London 120, Surrey 120, Somerset 112, and Leicestershire 103; the chief exceptions to a falling trend were rises in Devonshire 411 and Durham 118. The local trends of scarlet fever varied only slightly, the largest change being a fall of 23 in Yorkshire West Riding. The largest fluctuations in the returns for whooping-cough were a rise of 56 in Sussex and a fall of 58 in Lancashire. The notifications of diphtheria were 10 fewer than in the preceding week; the chief features of the returns were a rise of 3 in Warwickshire and in Staffordshire and a fall of 5 in Glamorganshire. Of the 15 cases of paratyphoid fever 9 were notified in Pembrokeshire, Haverfordwest R.D.

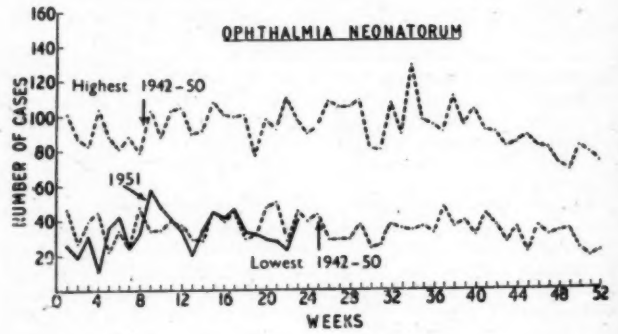
It appears that the seasonal rise in acute poliomyelitis has begun; the number of notifications increased from 28 to 52 during the week. The largest returns were Warwickshire 7 (Birmingham C.B. 5) and Yorkshire West Riding 5.

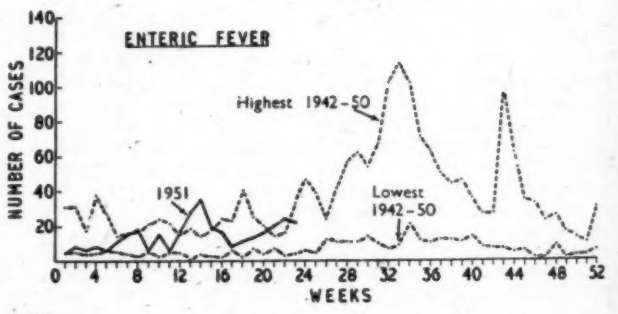
The incidence of dysentery still remains at a very high level. The chief feature of the returns during the week was a fall of 78 in the number of notifications in Middlesex. The largest returns were London 145 (Islington 53), Middlesex 92 (Ealing M.B. 35), Yorkshire West Riding 79 (Huddersfield C.B. 38), and Lancashire 76.

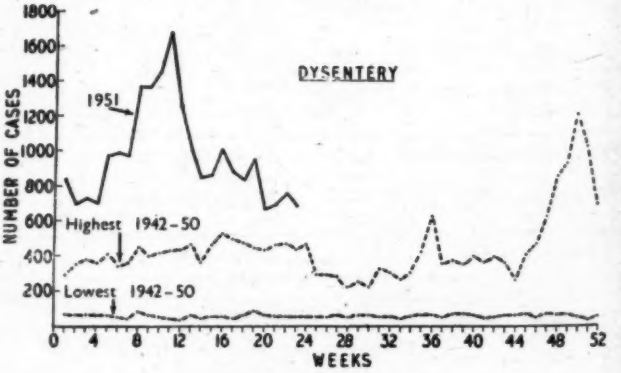
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported during the nine years 1942–50 are shown thus - - - - - -, the figures for 1951 thus ————. Except for the curves showing notifications in 1951, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Week Ending June 16

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 976, whooping-cough 3,290, diphtheria 29, measles 12,139, acute pneumonia 460, acute poliomyelitis 50, dysentery 509, paratyphoid fever 14, typhoid fever 10.

Medical News

International Congress of Clinical Pathology

The first congress will be held in London from July 16 to 20. The opening ceremony will take place at Friends House, Euston Road, N.W.1, at 3 p.m. on the first day, when Sir Lionel Whitby, President of the Association of Clinical Pathologists, will give an address on "The Science and Art of Medicine." The sessions will be divided into four main sections: Microbiology, Morbid Anatomy, Chemical Pathology, and Haematology. Members of the congress will be received by the Minister of Health at Lancaster House, and attend receptions given by the Royal College of Physicians, the B.M.A., the University of London, and the Goldsmiths' Company. Full details may be obtained from the Secretary-Treasurer, Dr. W. H. McMenemy, Maida Vale Hospital for Nervous Diseases, London, W.9.

Award to Mayo Clinic Scientists

The first $10,000 Dr. C. C. Criss award and gold medal for "outstanding contributions in the fields of public health and safety" were presented in Atlantic City on June 10 to last year's Nobel Prize winners, Drs. Edward G. Kendall and Philip S. Hench, whose joint efforts at the Mayo Clinic led to the development and use of cortisone for rheumatoid arthritis and other diseases. The presentation was made at the closing session of the annual meeting of the American Rheumatism Association. *(New York Times.)*

International Society of Orthopaedic Surgery

At the fifth congress of the Société Internationale de Chirurgie Orthopédique et de Traumatologie, held at Stockholm on May 21–25, the following officers were elected: President, Sir Harry Platt, Manchester; Vice-Presidents, Professor Etienne Sorrel, Paris, and Professor José Valls, Buenos Aires; Secretary-General, Dr. Jean Delchef, Brussels; Assistant Secretaries, Dr. P. Kempeneers, Brussels, and Dr. R. Van Cauwenberghe, Liége; Treasurer, Dr. M. Charles Parisel, Brussels. The president of the sixth congress, to be held in Switzerland in September, 1954, will be Professor Etienne Sorrel, assisted by Dr. Marcel Dubois.

King Edward's Fund Annual Meeting

The annual meeting of the Fund was held at the House of Lords on June 21, the Duke of Gloucester presiding. The Duke referred to various committees of inquiry set up by the Fund, and said that the findings of the inquiry into convalescent homes would soon be published. Part of the new programme of training schemes was now bearing fruit: the Nurses' Staff College was established two years ago and was doing valuable work; the Hospital Administrative Staff College was now in operation and the Minister of Health had paid tribute to its work; the School of Hospital Catering was also ready. In 1951 some £180,000 was being allocated in direct grants to hospitals and convalescent homes both within and without the Health Service. One after another of the homes for elderly sick were being opened and were receiving the support of the Ministry of Health. The Treasurer, Sir Edward Peacock, moved the adoption of the accounts and said that £197,100 had been absorbed by grants to hospitals and convalescent homes and over £103,000 spent on special services. A vote of thanks to the Duke of Gloucester was moved by the Speaker of the House of Commons and seconded by the Lord Mayor.

West Midlands Physicians Association

The second meeting of the association was held at the North Staffordshire Royal Infirmary, Stoke-on-Trent, on May 26. Dr. Bruce Maclean was elected president in succession to the late Sir Leonard Parsons.

North of England Obstetrical and Gynaecological Society

A meeting of the society was held in Newcastle on June 1 with the president, Dr. J. W. A. Hunter, in the chair. Mr. J. A. Hadley described a case of "Malignant Melanoma in Pregnancy"; Dr. James Hendry discussed "Prolonged Labour in Domiciliary Practice"; and Mr. Bryan Williams read a paper on "The Aetiology and Treatment of the Adherent Placenta."

Medical Section of the Library Association

On Wednesday, June 6, in connexion with the Library Association's annual conference in Edinburgh, Dr. L. W. Sharp, the Edinburgh University librarian, read an interesting paper to the Medical Section on "The Edinburgh Medical School in the Eighteenth Century." His outline of the early history of the Medical Faculty from its foundation in 1726 was illustrated by extracts from contemporary writings. In conclusion Dr. Sharp gave an account of various historical researches that are now being carried out on the period. Members of the Medical Section visited the libraries of the Royal College of Surgeons of Edinburgh, Royal College of Physicians of Edinburgh, and the Royal Medical Society.

W.H.O. Assistant Director-General Retires

Dr. Brock Chisholm, W.H.O. Director-General, announced on June 11 that Dr. Martha Eliot had given up her post with W.H.O. Dr. Eliot is one of the leading public health workers in the U.S.A. Before she joined W.H.O. in June, 1949, she was associate chief of the U.S. Children's Bureau. She had previously occupied other important posts in the American Government, and collaborated in large-scale child-health programmes in the United States and abroad. She will be replaced by Dr. Marcolino Gomes Candau, of Brazil. He joined W.H.O. a little more than a year ago. In his new job he will direct all the various services rendered by W.H.O. through public health teams, disease control demonstrations, consultants, training centres, and fellowships.

Association of Rheumatic Sufferers

In 1948 the British Rheumatic Association held its first annual general meeting in the Guildhall, having been in existence for a year; there were then 1,000 members, and two years later the number was doubled. The association is a registered charity; briefly its aims are to increase the facilities for early diagnosis and treatment, to collect information about the disease, and to promote public understanding of the problems and needs of rheumatic sufferers. Its efforts benefit those people as a group, only reserving certain personal services to its members. In hospitals with rheumatic units the waiting-lists are long, and many patients become disabled through the delay in obtaining treatment; many of the beds allocated to rheumatic cases are occupied for long periods by elderly disabled patients who do not need hospital service but for whom no other accommodation is available. It was to offset this problem that B.R.A. Homes, Ltd., was founded as a financially independent registered charity. The object is to provide accommodation both for patients who live too far away from a hospital with a rheumatic unit to travel daily for treatment and for those at present occupying beds in hospitals simply because they have nowhere else to go. The first hostel is to be at Northwood, about two miles away from the Mount Vernon Hospital, and will at first house 37 patients, with the possibility of increasing the number to 52. £12,500 is needed to finance the project, and the association hopes to interest the benevolent public and more especially industrialists. The foremost aim is a practical one—to treat early and enable patients to return to work as soon as possible. As the contributions paid by industry will be counted as welfare expenses, and therefore be tax-free, the project is economic as well as humane, since the loss to industry of workers suffering from rheumatism will be lessened.

Nuffield Foundation Dental Fellowships

The Foundation is prepared to award a number of fellowships and scholarships for two main purposes; first, to enable men and women with dental qualifications to receive additional training in pure and applied science which will fit them to follow an academic career in dentistry; secondly, to train university graduates in science and medicine to undertake research on dental health and disease. Further details and forms of application can be obtained from the secretary of the Foundation, 12 and 13, Mecklenburgh Square, London, W.C.1.

Public Health Laboratory for Leeds

The *Yorkshire Post* reports that a new Ministry of Health laboratory for public health bacteriological work is to be built in Leeds. Up to now this work has been done at the University; the establishment of the new laboratory will mean that the service can be extended to a much larger community.

Commemorating John Brownlee

The University Department of Infectious Diseases for Glasgow, under the charge of Dr. T. Anderson, will in the new year have its headquarters in the Ruchill Hospital. It is proposed to call the laboratories of the Department the John Brownlee Research Laboratory, to commemorate the name of one who did so much to apply statistical methods to the study of infectious diseases. It is proposed to place on the building a plaque commemorating John Brownlee, and it is hoped that his old associates and those interested in his work will contribute to the cost of this. Donations should be sent to Dr. T. Anderson, Infectious Diseases Department, Ruchill Hospital, Glasgow, Scotland.

COMING EVENTS

Banting Memorial Lecture

The Banting Memorial Lecture of the Diabetic Association will be delivered by Professor C. N. H. Long, of Yale Medical School, in the medical school of the Postgraduate Medical School of London, Ducane Road, W., on Friday, July 6, at 11.30 a.m. His subject is "Present Concepts of the Endocrine Control of Carbohydrate Metabolism." The lecture will be preceded and followed by lectures and demonstrations from 10.15 a.m. to 4.30 p.m. Admission is free and all interested are invited to attend.

British Social Biology Council

The annual general meeting of the council will be held at 2.30 p.m. on July 10 in the council chamber of the Free Church Council, 27, Tavistock Square, London, W.C.1. Dr. G. L. C. Bertram, director of the Scott Polar Research Institute, will speak on the relationship of population and food production. All interested in this problem are invited to attend.

Association of Surgeons

The Association of Surgeons of Great Britain and Ireland will hold an annual meeting in Manchester at the Medical School, July 19 to 21. Full details may be obtained from the secretary of the association, 45, Lincoln's Inn Fields, London, W.C.2.

International Congress for Psychotherapeutics

Under the auspices of the Nederlandse Vereniging voor Psychotherapie an international congress will be held at Leiden-Oegstgeest from September 5 to 8. The subject of the congress will be "The Affective Contact." Details may be had from the secretary of the Dutch Society for Psychotherapeutics, Psychiatric Clinic of the State University, Leyden.

Princess Tsahai Memorial Hospital

The hospital built in Ethiopia in memory of Emperor Hailé Selassié's daughter will be opened on July 23. To celebrate the opening a garden party will be held at the Holme (Bedford College), Inner Circle, Regent's Park, N.W.1, on July 10 from 3 p.m. to 10 p.m. Miss Wendy Hiller will open the bazaar, and Lord Winster will preside. Gifts for the refreshment and other stalls will be much appreciated, and should be sent to the Hon. Secretary, 3, Charteris Road, Woodford Green, Essex. Donations towards the cost of equipment for the hospital will be gratefully acknowledged by the Hon. Treasurers, Lord Horder and Lord Amulree, c/o Messrs. Gold and Prideaux, 88, Bishopsgate, E.C.2.

King Edward's Fund Homes for Aged Sick

In June, 1949, the Fund allocated £250,000 to the setting up of homes for the aged sick. These homes are for people who no longer need to stay in hospital yet need some hospital care. Twelve homes are planned; one has already been opened at Whittington, and the second will be opened by Lord Horder on July 4 at 2.30 p.m. It is "Westmoor," 244, Roehampton Lane, S.W.15, and is run by managers linked with the Battersea and Putney Hospital Management Committee.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Monday

INSTITUTE OF NEUROLOGY, National Hospital, Queen Square, London, W.C.—July 2, 5 p.m., *"Acalculia,"* Guest Lecture by Dr. F. Grewel (Amsterdam).

Tuesday

EDINBURGH POSTGRADUATE BOARD FOR MEDICINE.—At Edinburgh University (Anatomy Lecture Theatre), July 3, 4.30 p.m., *"Bone Growth, with Special Reference to the Epiphyses,"* by Professor H. A. Harris.

INSTITUTE OF NEUROLOGY, National Hospital, Queen Square, London, W.C.—July 3, 5 p.m., *"Treatment of Cerebral Embolism and Thrombosis,"* Guest Lecture by Professor René Leriche (Paris).

WEST END HOSPITAL FOR NERVOUS DISEASES, 40, Marylebone Lane, London, W.—July 3, 2.30 p.m., *"Orthopaedic Treatment in Neurology, with Special Reference to the Part of Orthopaedic Surgery in Spastic Paralysis."* Clinical demonstration in neurology by Mr. K. I. Nissen.

Wednesday

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, London, W.C.—July 4, 5 p.m., *"The Range and Results of Transurethral Surgery,"* Hunterian Lecture by Mr. A. Wilfrid Adams.

WEST LONDON MEDICO-CHIRURGICAL SOCIETY.—At West London Hospital, W., July 4, 5.30 p.m., annual general meeting.

YORKSHIRE SOCIETY OF ANAESTHETISTS. — At the General Infirmary at Leeds, July 4, 8 p.m., *"Methods of Anaesthesia in Chest Surgery,"* by Dr. L. Mountford.

Thursday

INSTITUTE OF NEUROLOGY, National Hospital, Queen Square, London, W.C.—July 5, 5 p.m., *"Intrathecal Tuberculin Reactions,"* Guest Lecture by Dr. Honor M. V. Smith.

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, London, W.C.—July 5, 5.30 p.m., *"Carcinoma of the Nasopharynx,"* Otolaryngology Lecture by Professor Kenelm. H. Digby.

Friday

DIABETIC ASSOCIATION.—At Postgraduate Medical School of London, Ducane Road, W., July 6, 11.30 a.m., *"Present Concepts of the Endocrine Control of Carbohydrate Metabolism,"* Banting Memorial Lecture by Professor C. N. H. Long (Yale Medical School). Preceded and followed by lectures and demonstrations from 10.15 a.m. to 4.30 p.m.

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, London, W.C.—July 6, 5 p.m., *"Oral Manifestations of Systemic Disease,"* Charles Tomes Lecture by Professor H. H. Stones.

ROYAL SANITARY INSTITUTE.—At Town Hall, Colwyn Bay, July 6, 10 a.m., papers: "*Co-operation Between the Various Services—Hospital Board and Local Authorities—in the Promotion of Health*," by Dr. D. J. A. Alban Jones; "*The Prevention of Food Poisoning*," by Dr. D. E. Parry Pritchard. Afternoon visit.

Saturday

SOUTH-EAST METROPOLITAN REGIONAL TUBERCULOSIS SOCIETY.—At Royal Pavilion, Brighton, July 7, 10.30 for 11 a.m., "*Treatment and End-results of Tuberculous Pyo-pneumothorax*," by Dr. Geoffrey Todd; "*Laboratory Aspects of the Tuberculosis Problem*," by Dr. J. E. Jameson.

APPOINTMENTS

BOWIE, DOUGLAS ST. JEAN, M.B., Ch.B., Medical Officer, Rhodesia Railways, Bulawayo.

EAST ANGLIAN REGIONAL HOSPITAL BOARD.—*Orthopaedic Registrar at Norfolk and Norwich Hospital*, L. W. Godfrey, M.B., B.S. *Surgical Registrars at Norfolk and Norwich Hospital*, R. M. T. Walker-Brash, B.M., B.Ch., F.R.C.S., and B. M. Corkill, M.B., Ch.B., M.R.C.O.G.

FISHER, G. R. C., M.B., B.Ch., Receiving Room Officer, West Kent General Hospital, Maidstone, Kent.

FISHER, S. W., M.D., D.I.H., Consultant to the National Coal Board, from June 1, for the period of one year.

HOSPITAL FOR SICK CHILDREN, Great Ormond Street, London, W.C.—*Assistant Medical Registrar (Registrar Grade)*, H. G. Dunn, M.B., M.R.C.P., D.C.H. *Assistant Morbid Anatomist (Senior Hospital Medical Officer)*, R. C. B. Pugh, M.D.

LIVERPOOL REGIONAL HOSPITAL BOARD.—*Whole-time Consultant Pathologist to Walton Hospital and City Hospital North, Liverpool*, H. E. Vickers, M.D. *Whole-time Assistant Radiotherapist to Liverpool Radium Institute*, W. R. Argument, M.B., B.S., D.M.R.T. *Whole-time Tuberculosis Medical Officer to Central Chest Clinic, Liverpool*, F. J. Welton, M.B., Ch.B., D.P.H. *Consultant Radiologist to Liverpool Stanley Hospital and Whiston County Hospital*, G. D. Scarrow, M.D., M.Rad., D.M.R.D. (appointed jointly with Board of Governors of United Liverpool Hospitals). *Whole-time Assistant Psychiatrist to Upton Mental Hospital*, J. D. Glynn, L.R.C.P.&S.I., D.P.M. *Whole-time Assistant Venereologist to Seaman's Dispensary, Liverpool*, A. S. W. Egerton, L.R.C.P.&S.Ed. *Whole-time Assistant Pathologist to Warrington Group of Hospitals*, D. B. Mossman, M.B., Ch.B. *Consultant Anaesthetist to hospitals in North and South Liverpool Groups*, J. D. Loughrey, M.R.C.S., L.R.C.P., D.A.

WHEELDON, FRANCIS TASKER, M.B., B.S., F.R.C.S., First Assistant, Department of Orthopaedics, St. George's Hospital, London, S.W.

WISE, L., M.B., Ch.B., Senior Lecturer in Chemical Pathology, University College of the West Indies.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Broadhead.—On May 22, 1951, at Newport, Isle of Wight, to Jill (formerly Moody), wife of H. H. Broadhead, M.B., B.Chir., a son.

Craig.—On June 17, 1951, at Bristol, to Dr. Jean Craig (formerly Simpson), wife of Dr. R. A. Craig, a daughter.

Currie.—On June 24, 1951, at The Knoll, Duns, to Morag (formerly Duncan), wife of Dr. Gordon Currie, a son.

McCrae.—On June 4, 1951, at Ayrshire Central Hospital, Irvine, to Eileen (formerly Crane), wife of John S. McCrae, M.B.E., M.B., Ch.B., Glenavon, Catrine, Ayrshire, a daughter.

Mellor.—On June 8, 1951, to Dr. and Mrs. Norman Mellor, of Cereal, Alberta, a daughter.

Roberts.—On June 18, 1951, at Westminster Hospital, London, S.W., to Mary (formerly Cook), wife of Dr. Peter Roberts, a son—Paul Morton.

Walters.—On June 6, 1951, at the Bromhead Nursing Home, Lincoln, to Daphne (formerly Pullein-Thompson), wife of Geoffrey A. Bagot Walters, F.R.C.S.Ed., a son.

MARRIAGES

Camac—Swift.—On June 16, 1951, at Church Gresley Parish Church, John Cramsie Camac, M.B., B.Ch., M.R.C.S., L.R.C.P., to Joyce Enid Swift.

DEATHS

Ainsley.—On May 29, 1951, at Middelburg, South Africa, William Ainsley, L.R.C.P.&S.Ed., L.R.F.P.S., of Downview Court, Worthing, formerly of Preston, Lancs.

Bellamy.—On June 22, 1951, at Cross Tree Cottage, Winterbourne Stickland, Dorset, Henry Francis Bellamy, M.D.

Essex-Lopresti.—On June 13, 1951, at 5, Reservoir Road, Olton, Birmingham, Peter Gordon Lawrence Essex-Lopresti, F.R.C.S.Ed., D.A., aged 36.

Francis.—On June 16, 1951, at 30, Brookfield Mansions, Highgate, London, N., Louis Arthur Francis, M.R.C.S., L.R.C.P., formerly of Uxbridge, Middlesex, aged 84.

Hopkinson.—On June 11, 1951, Emilius Hopkinson, C.M.G., D.S.O., M.B., B.Ch., of Wynstay, Balcombe, Sussex, late of Gambia, West Africa, aged 82.

Ingall.—On June 22, 1951, at The Hospital, Ashford, Kent, Frank Ernest Ingall, F.R.C.S., D.P.H., aged 81.

Johnstone.—On June 18, 1951, at Rosslyn Street, Brora, Sutherlandshire, Walter Edward Johnstone, M.B., C.M., J.P.

Lemon.—On June 18, 1951, at a nursing-home, Hove, Edward Henry Lemon, M.R.C.S., L.R.C.P., D.P.H., aged 85.

Manifold.—On June 15, 1951, in Saudi Arabia, John Alistair Manifold, O.B.E., M.R.C.S., L.R.C.P., Lieutenant-Colonel, R.A.M.C., aged 38.

Norman-Walker.—On June 18, 1951, at The Coombe, Streatley, Berks, John Norman Norman-Walker, C.I.E., M.R.C.P., Colonel, I.M.S., retired, aged 79.

O'Neill.—On June 16, 1951, in London, Hugh O'Hagan O'Neill, M.B., Ch.B.

Porter.—On June 22, 1951, at 61, Tavistock Drive, Nottingham, Frank Constable Porter, M.R.C.S., L.R.C.P., L.D.S., D.D.S., aged 83.

Richardson.—On June 19, 1951, at St. Andrews, Hugh Richardson, D.S.O., M.D., D.P.H., Colonel, A.M.S., T.A., retired, aged 77.

Williams.—On June 17, 1951, at Royal Naval Hospital, Chatham, Edward Rex Pascoe Williams, O.B.E., M.B., B.S., Surgeon Commander, R.N., aged 49.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Electric Shocks from Car Handles

Q.—*A young man consulted me recently complaining that every time he got out of his car and closed the door with his hand he received an electric shock. This did not repeat itself when he touched the door again. This has occurred to such an extent that he carefully uses his handkerchief when closing the door. I frankly thought that he was exaggerating until my wife started complaining about the same thing a week ago. (There is no psychological link-up as she knew nothing of this patient.) Not only does she "jump" with the shock but she states that she hears a hiss. What is the explanation?*

A.—This is a common phenomenon resulting from the accumulation of a static charge generated by certain moving parts in the vehicle and by friction between the rubber tyres and the road. This charge and, in consequence, the shock felt by a person standing on the road and touching, for example, a door-handle can be considerable, particularly on a hot dry day, although the shock is insufficient to cause injury. It is experienced on many public service vehicles, and to prevent shock to passengers boarding and alighting a special tyre with a metallic content has been developed so that the static charge may escape to earth. With some road vehicles, more particularly those propelled by steam engines, such as a road roller, the static charge can be quite large, and these vehicles are sometimes equipped with a length of light chain trailing on the road, to prevent the building up of the static charge.

Rapid Rh Testing

Q.—*Is there any quick and reliable clinical method of determining the Rh status when a transfusion is urgently required and the Rh group is not known? Methods employed hitherto are not suitable for use in the patient's own home or, indeed, in hospital as an emergency measure in the absence of a pathologist.*

A.—Before any blood transfusion it is desirable to determine the Rh group of the recipient, and this is essential in the case of a girl or woman (who may bear children or who may have borne children and developed anti-Rh antibodies).

Accurate Rh grouping, even in experienced hands, may be a long task, and a rapid method which will give no false positives and few false negatives in inexperienced hands has been much sought. The difficulties and dangers of domiciliary transfusion are great; if this is necessary in a "life and death" emergency it would be justifiable to use Rh-negative blood, although this is scarce. It would be better, if possible, to use dextran or small-pool or irradiated plasma, and then to transfer the patient for blood transfusion to a centre where there are facilities for grouping and direct compatibility tests.

Among rapid laboratory methods for grouping recipients, the capillary method of Chown and the slide technique of Diamond are the most popular. For the capillary method, now described in most standard works, the cells must be washed, and results are not entirely reliable in inexperienced hands.

Diamond's method has the advantage that whole blood (heparinized or oxalated) or a suspension of cells in their own (or neutral) serum is used: a cell suspension in saline or citrate is not suitable. One drop of whole blood and one drop of a strong incomplete anti-D serum of known performance are mixed together on a piece of opalescent

glass; the mixture is rocked gently over a lamp, care being taken not to let it become overheated and dried up at the edges. The cells agglutinate strongly in three or four minutes if the cells are Rh-positive; doubtful reactions should be classed as negative. Positive and negative controls are necessary; in a hospital laboratory suitable cells can be kept back from routine work for use as controls.

Another useful method requiring no special apparatus is this: One volume (about 0.01 ml.) of a strong saline anti-D serum, and one volume of an approximately 2% suspension of the patient's cells in saline, are mixed in a small tube (the rimless precipitin variety, external diameter 6.5 mm., used in routine Rh work is suitable); the tube is agitated in a 37° C. water-bath for 10 minutes, centrifuged for one minute, and the deposit is then spread on a slide and examined microscopically. Great care must be taken in removing the deposit from the tube not to break up the very delicate agglutinates. Clumps of cells mean that the sample is Rh-positive.

It must be stressed that "rapid" methods are liable to give false negative results, and so, while useful for grouping recipients in case of emergency, donors so grouped must never be used as "Rh-negative donors."

The dangers inherent in the rapid methods can be reduced considerably by practice and experience. Workers proposing to undertake emergency transfusions should spend a few hours regularly in becoming familiar with the practical details of the method they propose to adopt, such as storage of serum, in learning the "snags" and how to circumvent them, and in streamlining their technique—so important in an emergency when time is vital.

The questioner makes no mention of ABO grouping or a direct compatibility test: this last is the most important single test of all. Mixing a thin saline cell suspension with the patient's serum on a cold slide is valueless and creates a false sense of security. If cross-matching by a tube technique in an incubator really is impossible, and not just too much trouble, Diamond's technique is of some value: Mix one drop of the donor's whole blood with one drop of the recipient's serum on a piece of opalescent glass (or a slide) and rock over a lamp as for the rapid Rh test. This method can detect antibodies of the "incomplete" or albumin type.

B. asiaticus and Fatal Gastro-enteritis

Q.—*B. asiaticus was recently isolated from the stool of an infant aged 5 weeks who died of gastro-enteritis. The case appears to have been a sporadic one. Of what significance is this organism? Is it causative? Does the organism belong to the dysentery group?*

A.—*B. asiaticus* is now included in the paracolon group of organisms, though previously it was included in the proteus group. The paracolon group is intermediate between the food-poisoning and dysentery groups on the one hand and the coliform group on the other. The exact pathological significance of the paracolon group is difficult to assess though some types are known to cause intestinal disease in man. Studies on *B. asiaticus* have been conducted in sub-tropical countries, where it has been isolated as commonly from the faeces of healthy individuals as from those suffering from non-specific enteritis. Nevertheless some observers believe that this organism may cause an enteric-like fever. It is, however, a common experience to isolate a paracolon organism from a stool during convalescence from dysentery or gastro-enteritis, even when the causative shigella or salmonella type was found in almost pure culture during the acute stage of the disease.

Babies and young children are much more susceptible to infection by accepted intestinal pathogens than are older age groups, and it has been suggested that the paracolon group of organisms may cause infantile gastro-enteritis. Therefore *B. asiaticus*, whose ability to cause gastro-enteritis in adults is in doubt, may nevertheless be pathogenic to an infant of 5 weeks.

Muscle Building

Q.—*What is the value of the various physical culture courses which are designed to cause muscular hypertrophy?*

A.—It is always advisable, before recommending any course of physical culture, to make sure that it is based on rational anatomical and physiological considerations. Frequently, physical culture courses concentrate on the development of muscular hypertrophy without primarily considering the functions to which the muscles should normally be put. While physical training from an efficiently trained instructor is most useful in the development of correct posture and physique, there is little point in developing a large girth of muscle in the limbs if this cannot be usefully employed. One quite often sees enthusiastic "muscle builders" who are unable to carry out full respiratory and other physiological exercise in spite of their sustained efforts at muscular development.

Compulsive Yawning

Q.—*A Turkish lady of 48 has suffered since the age of 23 from attacks when she yawns loudly. The attacks begin without apparent cause, occur at two- to three-minute intervals, and may last for three to six months. The lady speaks but rarely during the attacks. Physical examination is negative. What is the diagnosis and treatment?*

A.—A pathological tendency towards yawning has not been described as a neurotic symptom. It does occur in certain brain tumours, but a history of 25 years without extension of the symptoms or the development of physical signs makes this possibility extremely unlikely. Yawning attacks can occur as an epileptic phenomenon, but they are then almost always associated with the involuntary voiding of urine, and followed by giddiness, headaches, and sometimes vomiting; some degree of changed consciousness should be observable, if in the case in question the attacks are due to cerebral dysrhythmia.

The most likely diagnosis in the patient described is post-encephalitic respiratory disturbance. S. A. Kinnier Wilson (*Neurology*, 1940: Arnold, London) mentions a personal case of post-encephalitic paroxysmal yawning which was remarkable for the noisy preceding inspirations; spasms in some cases have been violent enough to dislocate the lower jaw. Like other respiratory sequelae of epidemic encephalitis paroxysmal yawning can occur in the absence of other post-encephalitic signs.

No specific treatment is known; amphetamine sulphate or related drugs should be tried, the dosage being pushed to maximum tolerance; psychotherapeutic assistance with any emotional disturbances that might be present, and to which post-encephalitics are notoriously prone, should diminish the frequency of the attacks.

Yoghourt and Gastro-intestinal Disorders

Q.—*Is yoghourt of value in treating gastro-intestinal disorders? Is it possible to disguise its flavour? Are there any definite contraindications to its use?*

A.—As far as is known yoghourt has no specific value in the treatment of gastro-intestinal disorders. It is now sold by some dairies flavoured with fruit juices, which some people think make it more palatable. There are no definite contraindications to its use.

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON, W.C.1. TELEPHONE: EUSTON 2111. TELEGRAMS: *Aitiology, Westcent, London.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.
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